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LATE REACTIONS TO METALLIC FOREIGN BODIES*

THOMAS W. BOTSFORD, M.D.,† AND D. RICHARD FRENI, M.D.‡

WEST ROXBURY, MASSACHUSETTS

FEW military or civilian surgeons have allowed a wound to heal around a metallic foreign body without wondering what the eventual outcome would be. Will the foreign body migrate, act as a focus of infection or cause pain, or will it become encapsulated and cause no symptoms? Today, many veterans have foreign bodies imbedded in various regions of the body, and in the months since the cessation of hostilities, we have had the opportunity of studying and treating a few late reactions caused by such bodies. This communication presents observations on a group of 40 patients who have been treated at the Veterans Administration Hospital in West Roxbury, Massachusetts. The types of reactions encountered and their management are emphasized. It is of principal interest that each patient included in this study had a long and asymptomatic period between the date of recovery from the original wound and the onset of the symptoms for which he was hospitalized. Late reactions to foreign bodies are not a new phenomenon, for observations have been made concerning them after nearly all wars. However, the problem merits renewed interest because of its greater frequency and because of improved technic in the management of metallic foreign bodies and their complications.

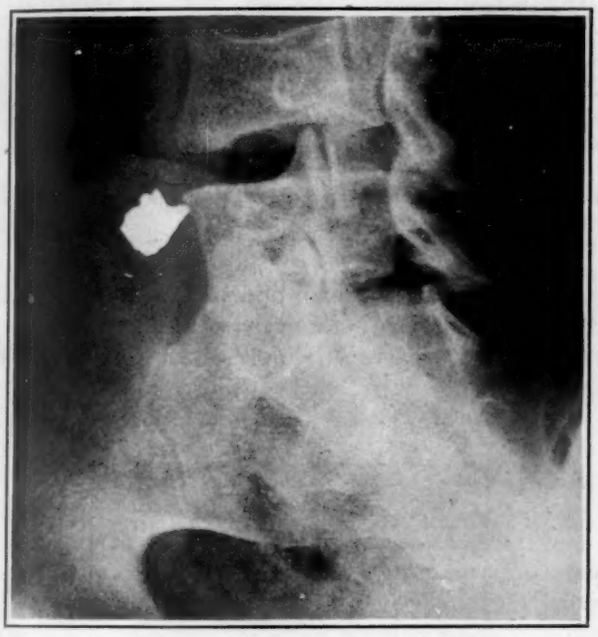

FIGURE 1. *Lateral Roentgenogram of Pelvis in Case 11, Showing Position of Foreign Body on August 7, 1946.*

FIGURE 2. *Anteroposterior Roentgenogram of Pelvis in Case 11, Showing Position of Foreign Body on August 7, 1946.*

When a nonabsorbable foreign body is imbedded in soft tissue it becomes gradually surrounded by a fibrous capsule.[1] If pathogenic micro-organisms are present and are uninhibited, an abscess and a chronically discharging sinus tract may be established; this reaction may be immediate or delayed,

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and its severity will depend on the virulence of the offending organism.[1] Foreign bodies may remain encysted for many years without causing symptoms, as in Paschal's[2] patient, who had an Indian arrowhead embedded in his chest wall for sixty-one years without symptoms. This case is an exception, because as a general rule the patient who knows that he has an imbedded foreign object is more apt to have symptoms than one who is not aware of having a foreign body.[3] Bizarre migrations of foreign bodies occur, and Christopher[4] has noted many unusual

FIGURE 3. *Lateral Roentgenogram of Pelvis in Case 11, Showing the Changed Position of the Foreign Body on April 9, 1947. The foreign body migrated from opposite the superior anterior edge of the fifth lumbar vertebra to below the level of the sacrum in a period of eight months.*

examples. Migration of foreign bodies usually occurs when the body is a sharp, narrow object such as a needle. However, 1 of our patients (Case 11) exhibited migration of a piece of shell fragment that was almost square (Fig. 1, 2, 3, 4 and 5). Michael[5] has described a characteristic type of histologic foreign-body reaction to high-explosive shell fragments, but he makes no mention of the clinical application of this finding.

Between June 1 and December 31, 1946, of 1269 patients admitted to this hospital for surgery, 40* presented symptoms referable to war wounds in which there were retained metallic foreign bodies. Of this group, we have selected 11 patients in whom the symptoms were unequivocally caused by imbedded foreign bodies. The information concerning these patients is summarized in Table 1. All the patients in this series were male veterans of World War II who had been wounded by enemy action. They were all in the third decade of life.

FIGURE 4. *Anteroposterior Roentgenogram of Pelvis in Case 11, Showing the Foreign Body to Have Migrated Laterally and Completely across the Right Sacroiliac Joint.*
This film was made on April 9, 1947. The migration occurred over a period of eight months.

Nine patients had foreign bodies imbedded in other regions of the body than those mentioned in the table. For purposes of simplification and since the foreign bodies were not causing symptoms, they

FIGURE 5. *Photograph of the Foreign Body (Shell Fragment) Removed in Case 11.*

were not included in the table. The patients were all psychologically stable men who had been separated from the service after all their wounds had healed. The foreign bodies in all cases except 1—

*Since this paper was submitted for publication 23 additional patients with foreign bodies have been seen, 11 of whom have had their foreign bodies removed. Six patients had infection associated with the foreign body, and 5 had pain.

a metal ring from an infantry pack — were shell fragments varying from 0.2 to 3 cm. in greatest length. The foreign bodies were all located in skeletal muscle, except 1 in the liver. Six were in the lower extremity, 1 in the chest wall, 1 in the buttock, 1 in the iliopsoas muscle, and 1 in the lumbar region.

The interval between the date of healing of the initial wound and the onset of secondary symptoms varied from five to seventeen months. This fact was of especial interest, since 7 patients presented signs and symptoms of infection, and only 4 had pain alone without infection around the foreign body.

Multiple Foreign Bodies, with Cellulitis

There were 3 patients in this group, each with multiple, minute, metallic fragments imbedded in the leg. The following case report is typical:

Case 3. S. M., a 24-year-old former infantryman, was admitted to the hospital complaining of chills, fever and swelling of the left leg of 24 hours' duration. In March, 1945, he had been wounded in both legs and in the abdomen by enemy action. The leg wounds had been closed secondarily and were firmly healed 2 months after the date of original trauma. Three months later, he had an attack of cellulitis of the left leg, which was treated by heat, elevation and parenteral administration of penicillin. He was asymptomatic until the time of admission, 16 months after the original injury.

Physical examination revealed a well developed and well nourished man who appeared acutely ill. The heart and lungs were normal. The abdomen was normal except for two well healed operative scars. The left leg, from the knee to the lower calf, was diffusely reddened and tender, with local edema. There was a long, irregular, well healed wound over the lateral aspect of the left leg.

The temperature was 103°F. by mouth, and the pulse 100.

Examination of the blood showed a white-cell count of 8900. A roentgenogram of the left leg revealed numerous small shadows of metallic foreign bodies (Fig. 6). The diagnosis was cellulitis and multiple foreign bodies of the left leg.

The patient was treated by bed rest, elevation of the left leg and hot moist packs to the inflamed area. Penicillin was given intramuscularly in doses of 40,000 Oxford units every 3 hours. Within 48 hours, the temperature and pulse had subsided to normal and there was rapid improvement in the area of cellulitis. The treatment was continued for 7 days, and the patient was discharged, asymptomatic, on the 9th hospital day. At that time, the leg appeared grossly normal except for the scars previously noted. Two months after discharge, he was readmitted with a recurrence of the local cellulitis process. He was treated in the same manner, being hospitalized for 8 days. Again, the presenting signs and symptoms cleared, and he has been symptom free for 4 months.

Table 1. *Pertinent Data in Patients with Embedded Foreign Bodies.*

Case No.	Age	Causative Agent	Type of Foreign Body	Date of Initial Wound	Symptom-Free Interval	Anatomical Location	Signs and Symptoms	Cultures of Foreign Body	Treatment	Result
	yr.				mo.					
1	29	Shell fragments	Multiple	12-2-44	17	Left thigh and leg	Fever, pain and cellulitis	None performed	Penicillin and local heat	Improvement
2	24	Shell fragments	Multiple	1-11-45	13	Left thigh	Fever, pain and cellulitis	None performed	Penicillin and local heat	Improvement
3	22	Shell fragments	Multiple	3-27-45	3 and 16, and 18	Left leg	Fever, pain and cellulitis	None performed	Penicillin and local heat	Improvement
4	26	Land-mine fragments	Single	2-27-45	7	Left foot	Pain and callus formation	None performed	Removal	Cure
5	27	Shell fragments	Single	11-10-44	12	Right thigh	Draining sinus	*Aerobacter aerogenes*	Removal	Cure
6	24	Shell fragments	Single	3-10-45	12	Right shoulder	Local pain	None performed	Removal	Cure
7	28	Machine-gun bullet	Single	8-12-44	12	Right chest wall	Local pain	No organism	Removal	Cure
8	27	Shell fragments	Multiple	4-4-45	9	Liver	Pain, fever and abdominal mass	Hemolytic streptococcus and *Staph. albus*	Incision and drainage	Improvement
9	24	Shell fragments	Multiple	11-13-43	16	Left leg	Pain	None performed	Removal	Cure
10	21	Shell fragments	Multiple	11-26-44	6	Right buttock	Abscess	*Staph. albus*	Incision and drainage	Improvement
11	27	Shell fragments	Single	11-13-44	9	Right iliopsoas muscle	Abscess and sinus tract	*Staph. albus*; *Pseudomonas aeruginosa.*	Incision and drainage; removal at second operation.	Cure

We were able to check the Army medical records of the patients and found that the original treatment had followed the same pattern in each case. Penicillin as well as tetanus toxoid had been administered to each patient at the time of the original definitive treatment, the penicillin being continued until the wounds showed no evidence of infection. We cannot satisfactorily explain why infection suddenly occurred around a foreign body months after the wounds had healed. The pathogenic organisms at fault may have reached the site either by the blood stream or lymphatic vessels, or may have been continuously present in a dormant state. No other sites of infection elsewhere in the body, such as furuncles, infected teeth and foot infections, were found as exciting causes.

The patients are classified in three clinical groups, which are discussed separately and are as follows: multiple regional foreign bodies, with cellulitis; single or multiple foreign bodies, with abscess formation; and single foreign body, without infection but with pain.

None of the foreign bodies were removed because of their minute size and great number, but the patient responded rapidly to local treatment and penicillin as did 2 patients with similar foreign bodies (Cases 1 and 2). These patients represent a problem in that the foreign bodies are too numerous to remove and yet act as foci for occasional explosive infections. Between attacks there has been no swelling of the leg or evidence of chronic infection as far as the patients could tell. We could find no lesions on the feet that might have been a portal of entry for pathogenic organisms, although that is a likely explanation for this type of clinical course. Undoubtedly, with multiple foreign bodies such as these, considerable scar tissue is present, as well as interference with the local flow of lymph so that any micro-organism entering the leg tends to localize in the damaged region. No bacteriologic studies were made in Case 1 since we did not feel justified in opening an area of cellulitis.

FIGURE 6. *Anteroposterior and Lateral Roentgenograms of Left Leg in Case 3, Showing Multiple Foreign Bodies. These were associated with recurrent bouts of cellulitis.*

SINGLE OR MULTIPLE FOREIGN BODIES, WITH ABSCESS FORMATION

There were 5 patients who had localized infection caused by a foreign body. A typical case is the following:

CASE 8. M. M. S., a 27-year-old former infantryman, was admitted to the hospital on May 29, 1946, complaining of pain in the right upper quadrant, and of vomiting of 1 week's duration. On April 4, 1945, he had suffered a penetrating wound of the epigastrium and lacerations of the left lobe of the liver, right dome of the diaphragm, transverse mesocolon, stomach and jejunum. The wounds had been sutured, and at operation a shell fragment had been found in the jejunum and removed. The patient had been discharged from the service in August and had been asymptomatic for 9 months. He had spent no time in the tropics or the South.

Physical examination revealed a moderately obese man who appeared acutely ill. A firm, tender mass, measuring 20 by 20 cm., was located about half in the right upper quadrant and half in the epigastrium from the left upper quadrant. The remainder of the physical examination was negative.

The temperature was 101.4° F. by mouth, the pulse 88, and the respirations 20.

Examination of the blood disclosed a white-cell count of 15,000, and urinalyses were normal. A plain film of the abdomen showed several small shadows consistent with metallic fragments in the region of the left lobe of the liver. The diagnosis was pyogenic liver abscess caused by foreign bodies.

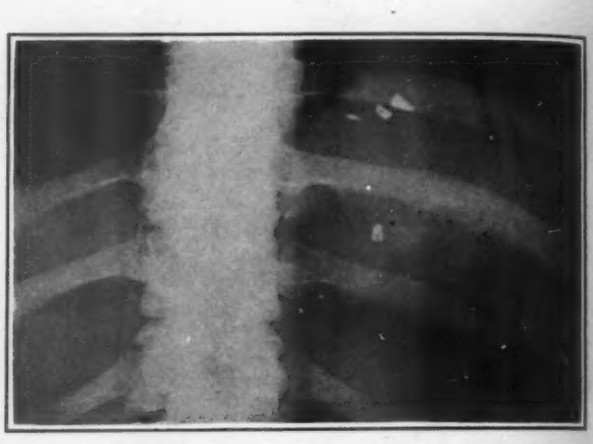

FIGURE 7. *Anteroposterior Roentgenogram of the Upper Abdomen in Case 4, Showing Two Foreign Bodies in the Region of the Left Lobe of the Liver. (The Other Radio-Opaque Shadows Represent Silver Hemostatic Clips.)*

The initial treatment consisted of bed rest, local heat to the abdomen and penicillin (30,000 Oxford units intramuscularly) every 3 hours. Two weeks after entry a large abscess of the left lobe of the liver was drained through an incision in the left upper quadrant. Cultures of the pus revealed hemolytic streptococci and *Staphylococcus albus*. No amebas were present either in the pus or in the stools. After drainage of the abscess, the temperature returned promptly to normal. The penicillin, however, was continued for 3 weeks.

He was discharged improved on July 13 but returned 11 days later with a recurrence of the liver abscess. X-ray films at that time showed that instead of five foreign bodies, there were only two (Fig. 7). Drainage was again established, and penicillin again administered. The wound was allowed to close very slowly so that no pocket could develop, and at the end of 11 weeks the patient was discharged. Nine months later he was asymptomatic and without signs of active infection. No foreign bodies were removed at either of these operative procedures. It is probable that several of the small foreign bodies were extruded with the pus that was drained.

In this case the location of the foreign bodies in the liver made their management complicated because of technical difficulties. Even with a Berman locator, these small, deeply situated foreign bodies are difficult to find and remove. In superficial abscesses, such as those in Cases 5 and 9, the foreign

body was removed, since it was not difficult to locate. In Case 10, we were not able to locate the foreign body at the time of drainage of the abscess, and at that time the Berman locator was not available.

Single Foreign Body, without Infection

The last group consisted of patients who had pain and discomfort referred to the presence of a foreign body, but did not have signs of infection. The following is a typical case:

Case 7. I. G. L., a 28-year-old former medical corpsman, was admitted to the hospital on September 6, 1946, complaining of pain in the right pectoral region of 1 year's duration. On August 12, 1944, he had been wounded in the right pectoral region by an enemy machine-gun bullet. He was hospitalized for 25 days and returned to duty with the wound healed. He was symptom free for 1 year and then began to have pain in the right pectoral region, especially when he used his right arm at work as a machinist.

Physical examination was negative except for a healed wound 3 cm. long. and just lateral to the right nipple. There was a diffuse area of thickening beneath the scar measuring 6 by 6 cm., which was tender to palpation.

Anterior and lateral roentgenograms of the chest revealed a ring-shaped foreign body (Fig. 8 and 9), which was removed under ether anesthesia. The object was firmly encapsulated in the pectoralis major muscle and was found to be a ring from an Army pack. Cultures of the area showed no growth. The wound healed by first intention, and the patient was discharged on the 8th postoperative day. He has been asymptomatic since removal of the foreign body.

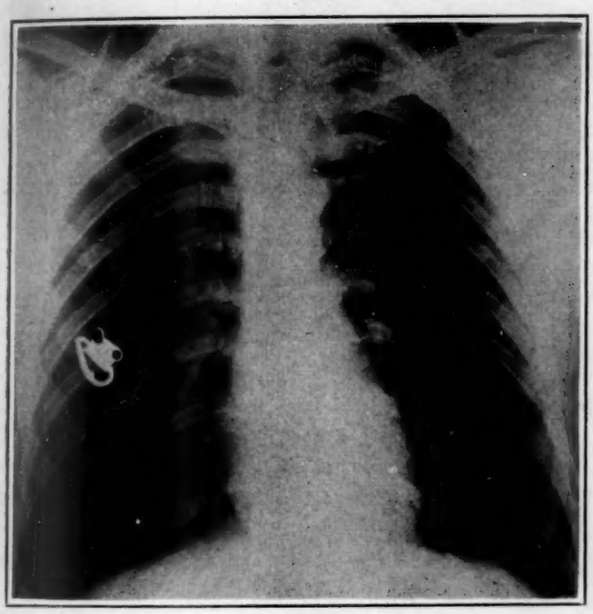

Figure 8. *Anteroposterior Roentgenogram of Chest in Case 7, Showing the Shadow of a Metallic Ring Embedded in the Anterior Portion of the Chest Wall.*

The treatment of this type of foreign-body reaction may be very simple or may present a most complex problem. It is difficult to determine whether the pain is due to the damage and cicatrix of the original wound alone or to the wound in addition to the retained foreign body, or whether the patient merely knows that a foreign body is present. In Case 7 the location and size of the foreign body undoubtedly accounted for the major part of the symptoms, since the pain occurred in the right pectoral region when the patient raised his right arm or did any strenuous work with the right upper extremity.

Discussion

In military surgery, bullets or shell fragments are not usually removed at the time of the initial treatment of the wound or even later unless one or more of the following indications are present: that the foreign body is easily found because of its size or location; that it is impinging upon a nerve, blood vessel, tendon, joint or bone; that it is a hazard to life or normal function because of its anatomic location; that it is the cause of pain; or that it acts as a focus of infection. The surgery of foreign bodies includes the entire field of general surgery and all the surgical specialties, and with rare exceptions, it is axiomatic that a foreign body is always more difficult to find and remove than is at first apparent.

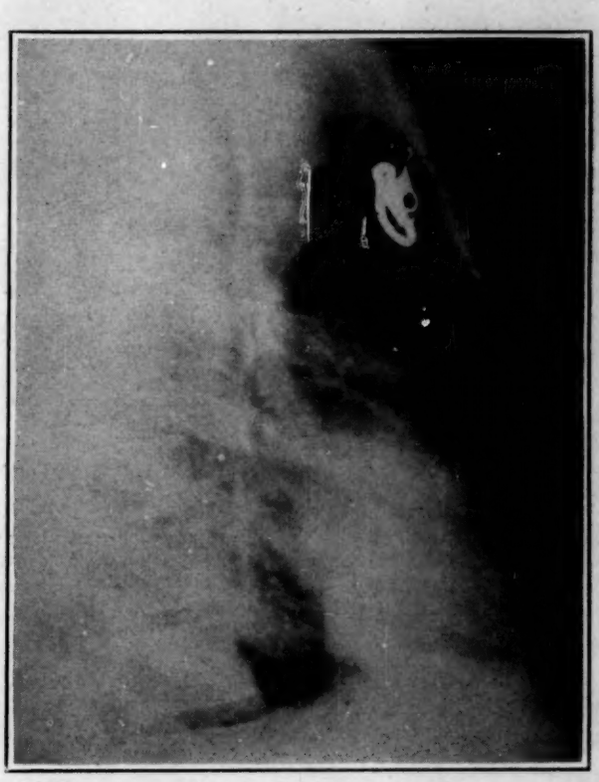

Figure 9. *Lateral Roentgenogram of the Chest in Case 7, Showing the Shadow of the Metal Ring Embedded in the Right Anterior Portion of the Chest Wall.*

In this communication we have emphasized the late reactions that may result from foreign bodies in soft tissues, the majority of which become encapsulated with fibrous tissue and cause no symptoms. A variable number of these patients, however, present the problem of infection and pain many

months after the wound has apparently healed. The management of these cases is not at all simple, since the foreign bodies may be small and so numerous, as in the first group discussed above, that removal is not feasible or even wise. If each fragment were removed the trauma of the operation would be extreme. On the other hand, when there is only a single foreign body its removal can be carried out in spite of technical difficulties, and if there are symptoms attributable to this foreign body, removal is necessary in most cases.

A plan for the management and study of these problems includes the basic principles of foreign-body surgery. In the first place the history and physical examination are carefully evaluated to determine the part the foreign body may play in the clinical picture. It must be remembered that the injury of the tissues may be the cause of the symptoms and that the foreign body itself may be only an innocent bystander. A review of the Army medical record is helpful in this respect. Secondly, roentgenologic studies of the location of the fragment are essential before any attempt of removal is made. Thirdly, a decision must be made whether or not to administer penicillin or sulfadiazine. Our policy has been to give penicillin to patients who present signs of infection as soon as they enter the hospital. In cases in which there is no sign of infection and removal is contemplated, penicillin is started on the day prior to operation and continued until the wound is healed. We have given booster doses of tetanus toxoid in all cases. Fourthly when removal of the foreign body is performed, the entire fibrous capsule is removed with the foreign body. Histologic study of the excised material to determine the presence or absence of other foreign matter, such as cloth, should be carried out, in an attempt to prove or disprove the presence of nonopaque material as a factor in the presenting symptoms. Finally, anaerobic and aerobic cultures of the foreign body are made in the operating room. Careful bacteriologic studies in these cases may do much to clarify the late septic reactions. In patients who have multiple small fragments with cellulitis, such as those in the first group discussed above, special attention should be paid to the search for lesions elsewhere, — for example, foot infections, — which may be the portal of entry for intermittent explosive infections.

The basic principles of foreign-body surgery are accurate localization and the control of infection. No attempt at surgical removal should be made until these two factors are properly considered. The use of antibiotics, sulfonamides, tetanus immunization and antitetanic serum have made the surgical technic in these potentially infected, if not actually septic, wounds much safer.

The most accurate localization of the foreign body prior to surgical procedures is paramount. Every surgeon knows that a search for a seemingly easily accessible foreign body may end in failure. The necessity of accurate localization has led to many an ingenious method of using the roentgenogram and fluoroscope. Films made in two planes with skin markers and two-needle localization under fluoroscopic control are common methods of localization. Reid and Black[6] have described methods of roentgenologic localization. Removal of radiopaque foreign objects under direct fluoroscopic control is excellent in such regions as the hand and foot, but prolonged exposure of the patient and the operator to the roentgen rays must be carefully guarded against. The Berman "locator" introduced by Moorhead[7] is a surgical divining rod for accurate localization of metallic foreign bodies. It is simple to use, is a sensitive instrument and should be part of the standard armamentarium for surgical removal of metallic foreign bodies. From our experience we are convinced that the "locator" is an important contribution to this particular field of surgery. With the aid of the "locator," the search for the foreign body is greatly shortened in time, and much trauma is avoided. In Case 2 the piece of shell fragment had migrated to the right psoas muscle and was adjacent to the right iliac vessels and the right ureter (Fig. 1, 2, 3, 4 and 5). The "locator" pointed exactly to the metallic object, the search for which would have been prolonged, dangerous and even unsuccessful in spite of its fairly large size. An attempt to remove the same foreign body had ended in failure several months before.

Summary

The problem of late reactions to metallic foreign bodies is presented because of the increase in its incidence after World War II and because of the improvement in its management.

It is probable that there will be an increasing number of such cases in the next few years. Observations on the operative treatment on 11 patients out of a total of 40 are presented, showing that the reactions may be classified into three groups: multiple regional foreign bodies, with cellulitis; single or multiple foreign bodies, with abscess formation; and single foreign body, with local pain. A plan of management is outlined in which the importance of accurate localization and control of infection is stressed.

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CAPILLARY FRAGILITY AND DIABETIC RETINITIS*

With a Note on the Use of Rutin

RAFAEL RODRIGUEZ, M.D.,† AND HOWARD F. ROOT, M.D.‡

BOSTON

AN INCREASED incidence of retinal changes among patients with diabetes has been noted in recent years. Diabetes of long duration has been associated with the greatest increase in retinal hemorrhages, although hypertension or other evidences of generalized vascular or renal disease may be present or develop subsequently. The importance of this subject is well known to students of diabetes and to internists, who see increasing numbers of diabetic patients, old and young, with impaired vision from this cause.

The term "capillary vessels" includes the endothelial tubing that lies between the arterioles and the small veins. There is no marked distinction between the smallest capillary arteries, the capillary itself and the venules — Lewis calls them collectively "minute vessels."

The explanation of the cause and nature of increased capillary fragility is obscure. A careful discussion of the skin manifestations is given by Peck and Copley.[1] This phenomenon may occur under a variety of circumstances. Poisons, metabolic substances and vitamin deficiencies directly affect the endothelium. Physiologic variations affect the tonus of the capillaries or indirectly damage the endothelium. Capillary permeability is said to be increased in tuberculosis and in some diseases of the skin. In 1944 the capillary fragility in 18 per cent of 265 selected cases of hypertension was found by Griffith and Lindauer[2] to be increased. Persons with abnormal indexes were believed to be predisposed to retinal and cerebral hemorrhages. Patients with high blood pressure, when treated with thiocyanate, developed a further increase in fragility. Beaser[3, 4] studied the capillary fragility in diabetic subjects; the test showed a greater incidence of increased capillary fragility in patients in the fifth and sixth decades and in those with hypertension. Paterson[5–7] discussed capillary rupture with intimal hemorrhages in the causation of cerebral vascular lesions and studied also the vascularization and hemorrhages of the intima of arteriosclerotic coronary arteries.[8] Low capillary resistance was found in 30 of 120 diabetic patients in the University Hospital at Ann Arbor, Michigan, and diabetic retinitis proved to be the most frequently associated abnormality in such cases.[9]

In vitamin C deficiency it is supposed that the loss of the intercellular cement permits extravasation. A relation between low ascorbic acid content in the blood plasma and strength of the cutaneous capillaries in healthy children was seen by Ahlborg and Braute.[10] Greene[11] evaluated the capillary-resistance test in the diagnosis of subclinical scurvy and concluded that a positive reaction does not necessarily denote an insufficient vitamin C intake. At the New England Deaconess Hospital Sebesta, Smith, Fernald and Marble[12] determined the vitamin C blood level of 77 adults with diabetes and found both normal blood values above 0.8 mg. per 100 cc. and an excretion of the urine of more than 400 mg. of ascorbic acid in response to a 1000-mg. dose given intravenously. To test the possible relation between vitamin C in the blood and capillary fragility in these patients, a series of simultaneous determinations were made, and it was evident that no relation appeared between the vitamin C content of the blood and the capillary fragility.

Scarborough and Stewart[13] claim that the administration of hesperidin can reduce the number of hemorrhages in patients with vitamin P deficiency. The existence of vitamin P was postulated in 1936 by Szent–Györgyi,[14] who claimed that extracts of Hungarian red pepper and lemon juice contained a substance called citrin or vitamin P.

Studying the deficiency of vitamin C and vitamin P in man, Scarborough and Stewart state that administration of vitamin P does not control the large subcutaneous hemorrhages characteristic of the scorbutic state; these hemorrhages were arrested within twenty-four hours by large doses of ascorbic acid. Vitamin P can produce an increased capillary resistance in the scorbutic subject either before or after treatment with vitamin C. The authors believe that a deficiency of this vitamin may exist in man even after large doses of vitamin C.[15] At the moment it must be admitted that evidence for the clinical value of vitamin P in the absence of a deficiency of this vitamin is scanty.

Rutin, another flavone glucoside, is believed to influence capillary fragility. Rutin is a rhamoglucoside of queracitin, a derivative of flavanol. It is a tasteless, yellow, nontoxic powder, consisting of masses of microscopic needle-like crystals.[16] Both rutin and hesperidin are constituents of plants — garden rue, tobacco and so forth — and are similar in structure. The chemistry of both is

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described by Couch, Naghski and Krewson,[17] of the Eastern Regional Research Laboratory in Philadelphia. Rutin was first isolated from tobacco. The glucoside was prepared from the flure-cured type of high quality. It was expensive, but the cost is now within the reach of most patients. In an attempt to find a still more economical source of the drug, a number of plants were examined for rutin content, and buckwheat was discovered to be the most promising source.[17]

Several reports have indicated that rutin restores abnormal capillary fragility. Griffith, Couch and Lindauer[18] gave rutin in cases of hypertension, without toxic effects that could be attributed to rutin; nor was there any significant change in blood pressure, and capillary fragility became normal in 8 patients within two months of the beginning of medication. The authors also studied the relation between rutin and crude hesperidin in hypertensive subjects with increased capillary fragility.[18]

Shanno[19] considered rutin more efficacious than hesperidin. He recommended its use in cases of hypertension to maintain normal capillary fragility to prevent vascular accidents. A remarkable change in the character of the bleeding of patients with hereditary hemorrhagic telangiectasia was observed by Kushlan[20] after rutin therapy. These reports indicated that rutin is the most active of chemically related compounds that over the past years have been extracted from various plants. One should consider the use of rutin in any condition associated with an increase of capillary fragility.[21, 22]

Since this botanical drug became available for the treatment of abnormal capillary fragility, we have used it in several cases in which there was evidence of diabetic retinitis and high degrees of capillary fragility. Our studies show that capillary resistance is definitely low in practically all persons with diabetic retinitis. We suggest the desirability of further trial of this substance. More important, however, is the possibility that through further investigation of the pharmacology of rutin, we may ascertain the indications of its early use, in the hope of preventing the capillary damage related to the retinal and perhaps other degenerative complications in subjects with diabetes of long duration.

Methods of Determination of Capillary Fragility

The correct determination of capillary fragility is essential in the selection of patients for rutin therapy. Peck and Copley[1] discussed a considerable variety of methods by which capillary fragility may be tested, including the suction or negative-pressure method, the positive pressure based on the Rumpel–Leede phenomenon, the direct microscopical observation of the vessel at the end of the nail bed, the puncture and bleeding tests, and the skin tests that employ snake venom.

In measuring capillary resistance, we must consider possibly conflicting results due to differences in technics used by various workers. Cutter and Marquardt[23] studied capillary fragility on the end of the nail bed. Moloney,[24] studying capillary fragility in the newborn, used the negative-pressure resistometer. Beaser[3] concluded that negative-pressure methods are unreliable and that positive-pressure tests, such as Göthlin's method, are commendable. Greene[11] chose the Göthlin method when studying subclinical scurvy. Griffith et al.,[2] of the Eastern Regional Research Laboratory, employed the Göthlin technic in their interesting investigation of hypertension. This procedure requires only a blood-pressure cuff, a magnifying glass and a good light. In the present report we followed the Göthlin positive-pressure test, the technic of which is as follows:

> A circular area, 6 cm. in diameter, is marked in each antecubital space.
>
> A standard blood-pressure cuff is placed on the arm and a pressure equivalent to 35 mm. of mercury is maintained for fifteen minutes. The pressure is lowered, and all the petechiae within the circular area are counted, a good magnifying lens being used.
>
> The process is repeated on the other arm, a cuff pressure equivalent to 50 mm. of mercury being employed for the same period. The pressure is lowered, and the findings are noted.
>
> To determine the petechial index, the number of petechiae in the first stage is multiplied by 2, and the number accumulated in the second stage is added. The normal index is 8 (or less); an increased value is 13 (or more), and a borderline (probably increased), 9 to 12.

The present communication is concerned with results of the test for determining the capillary fragility in diabetic patients at the New England Deaconess Hospital. The findings reported deal with three groups of patients: nonselected diabetic patients; diabetic subjects selected with varying degrees of retinopathy; and patients with diabetic retinitis or retinitis proliferans and high degrees of capillary fragility who were treated with rutin.

Material and Method

One hundred unselected young and old diabetic patients, male and female, with short and long durations of the disease, with and without complications, who were routinely studied in the hospital wards and in a diabetic nursing home, had a measurement of capillary fragility by the petechial index of Göthlin, described above.

In 56 selected patients with diabetic retinopathy, the capillary fragility was studied by the same petechial index, with certain minor modifications.*

*To save time in these 56 patients the blood-pressure cuff was placed on both arms at the same time.

Rutin* was administered to 70 patients with retinitis and increased capillary fragility, only 20 of whom were adequately followed. The initial dose of rutin was 20 mg. three times a day; in the 20 patients adequately followed, the dosage was increased to 40 or 60 mg. three times a day.

In all the 156 patients the history was taken and physical examination performed by various members of the medical staff. The presence of retinitis was ascertained by careful ophthalmoscopic examination. In the patients under rutin therapy, the examination was followed by the ophthalmologist, and special attention was paid to the retinal damage and the visual field.

Results in 100 Unselected Diabetic Patients

The capillary fragility was found to be increased in 40 patients (40 per cent), borderline in 4 (4 per cent) and normal in the remaining 56 (56 per cent).

Increased Petechial Index

Diabetic retinitis and hypertension† were the most closely related abnormalities among the 40 patients with increased capillary fragility (Table 1).

Table 1. *Abnormalities in Diabetic Patients with Increased Capillary Fragility.*

Abnormality	No. of Patients	Percentage
Retinitis with normal blood pressure	14	35
Retinitis with hypertension	12	30
Hypertension only	11	27
Normal fundi with normal blood pressure	3	7.5

The relation of increased capillary fragility to retinitis and hypertension is remarkable. In consideration of this fact, we must mention again the similar results reported by Griffith and Lindauer,[2] Beaser,[3] Rudy and Beaser[4] and Wilder.[25] The following is a review of this group of 40 diabetic subjects in whom the capillary fragility was found to be abnormal.

Retinitis with normal and high blood pressure. Twelve patients (30 per cent) with increased petechial counts had retinitis with hypertension and 14 (35 per cent) had retinitis with normal blood pressure. Table 2 lists the 26 diabetic patients with retinitis with and without hypertension. Among these patients, 13 were women, and 13 men. Six male patients had retinitis proliferans, and in only 2 female patients was this severe degree of retinopathy observed. In the whole group of 8 cases with retinitis proliferans the blood pressure was normal in 2 and above 150 systolic, 90 diastolic, in the remaining 6. Five were men under the age of forty with long duration of diabetes. In all 26 patients, 15 were over and 11 under forty years of age. The duration of diabetes was eighteen and a third years in the younger and only thirteen and a fifth years in the older group.

Retinitis with hypertension only. Table 3 presents 11 cases in which hypertension was present with an increased capillary fragility but in which no retinal damage was observed.

Griffith and Lindauer[2] found low capillary resistance in 18 per cent of 265 cases of hypertension. In our group of nonselected diabetic persons, the incidence of poor capillary resistance with hypertension was 27.5 per cent. The patients were in most cases women in the fifth, sixth or seventh decade of life and with long duration of diabetes. It should be noted regarding the patients in this group that further examination of the fundi must be done over an extended period to observe any changes, especially in cases like the first patient listed in Table 3, a woman aged twenty-nine with diabetes of long duration who showed normal fundi but had hypertension, edema, moderate albuminuria and capillary fragility of 82 petechiae.

Table 2. *Pertinent Data in 26 Diabetic Patients.*

Case No.	Age	Sex	Duration of Diabetes	Fundoscopic Examination	Blood Pressure	Capillary Fragility
	yr.		yr.			
2962	36	F	23	Retinitis	Normal	64
2931	29	F	23	Retinitis	Normal	128
28608	49	F	16	Retinitis	Normal	118
12974	62	F	16	Retinitis	Normal	48
24586	23	F	13	Retinitis proliferans	Normal	300
17011	21	F	8	Retinitis	Normal	77
—	58	F	—	Retinitis	Normal	39
8973	51	F	26	Retinitis	High	101
5723	62	F	24	Retinitis	High	18
23711	54	F	7	Retinitis proliferans	High	41
22702	65	F	3	Retinitis	High	100
28396	65	F	1	Retinitis	High	48
—	58	F	—	Retinitis	High	44
19943	51	M	27	Retinitis	Normal	500
17943	55	M	23	Retinitis	Normal	95
28403	69	M	8	Retinitis	Normal	21
19102	66	M	9	Retinitis	Normal	210
29771	46	M	10	Retinitis	Normal	47
—	51	M	2	Retinitis	Normal	90
4768	32	M	23	Retinitis proliferans	High	24
11077	26	M	22	Retinitis proliferans	High	74
4162	29	M	22	Retinitis proliferans	High	19
27728	39	M	19	Retinitis proliferans	High	141
229020	31	M	9	Retinitis proliferans	High	32
12523	23	M	12	Retinitis	High	66
14044	66	M	10	Retinitis proliferans	Normal	115

Table 3. *Pertinent Data in 11 Diabetic Patients.*

Case No.	Age	Sex	Duration of Diabetes	Condition of Fundi	Blood Pressure	Capillary Fragility
	yr.		yr.			
8969	29	F	16	Normal	High	82
28626	70	F	1	Normal	High	14
—	62	F	—	Normal	High	110
—	56	F	—	Normal	High	90
11562	40	F	21	Normal	High	20
—	64	F	—	Normal	High	74
28400	67	M	10	Normal	High	23
28501	64	F	32	Normal	High	18
28522	48	F	1	Normal	High	17
29073	59	F	2	Normal	High	16
24210	79	F	3	Normal	High	135

*Obtained from the Eastern Regional Research Laboratory, Philadelphia.

†By hypertension is meant a blood-pressure reading of over 150 systolic, 90 diastolic.

Increased capillary fragility with normal fundi and normal blood pressure. In 3 cases (7.5 per cent) abnormal capillary fragility was found in patients with normal blood pressure and normal fundi (Table 4). The first 2 patients were ambulatory women with uncomplicated diabetes admitted for routine check-up. The third, a sixty-seven-year-old woman with diabetes of forty years' duration, was admitted as an emergency in mild acidosis and hematemesis of unknown origin (x-ray studies of the gastrointestinal tract and gastroscopy were negative, and coagulation and prothrombin time were normal, but the gastric acidity, as is often observed in

TABLE 4. *Pertinent Data in 3 Diabetic Patients.*

Case No.	Age	Sex	Duration of Diabetes	Condition of Fundi	Blood Pressure	Capillary Fragility
	yr.		yr.			
24872	48	F	29	Normal	Normal	14
27565	47	F	4	Normal	Normal	14
6562	67	F	40	Normal	Normal	48

diabetic patients, was below the normal limits); she had also an ulcer in a neurotrophic right foot and the Göthlin count showed 48 petechiae. Later, other youthful diabetic patients showed increased capillary fragility when no evidence of arteriosclerosis could be demonstrated by x-ray examination of the aortic, pelvic or leg arteries. This group of young adults (twenty-five to thirty years of age) confirm the judgment that increased capillary fragility may be present in young persons with diabetes of long duration as one of the earliest signs

TABLE 5. *Pertinent Data in 4 Diabetic Patients.*

Case No.	Age	Sex	Duration of Diabetes	Condition of Fundi	Blood Pressure	Capillary Fragility
	yr.		yr.			
23234	74	M	25	Normal	High	12
—	41	F	5	Normal	Normal	12
28435	64	F	1	Normal	Normal	10
8246	69	F	17	Retinitis	High	11

of arteriosclerosis, which will subsequently be manifest in nephritis, hypertension and so forth, and general arteriosclerosis.

Borderline Petechial Index

Griffith and Lindauer[2] found the petechial index to be borderline in 3 cases among a group of 265 cases of hypertension studied. They judge from the occurrence of complications that the borderline group should be called abnormal. In this series of unselected diabetic persons, the capillary fragility was classified as borderline in only 4 cases. Table 5 lists these 4 cases. Two had normal fundi with blood pressures above normal; the duration of diabetes was five years in one and twenty-five years in the other. A woman aged sixty-nine with diabetes of seventeen years' duration and with hypertension and retinitis is in this group of borderline cases. The use of rutin is suggested in diabetic patients whose petechial counts appear to be borderline.

Normal Petechial Index

Among the 56 diabetic patients of this nonselected group who had normal counts, in 54 the fundi were normal and only in 2 cases was retinal damage present. A twenty-two-year-old girl with diabetes of fourteen years' duration (Case 28922) and with retinitis proliferans, hypertension, nephritis, gangrene in the right foot, anasarca and uremia had a petechial index of 7. A seventy-three-year-old woman with retinitis proliferans and normal blood pressure (Case 46334) had only 3 petechiae. In a summary of this group of 100 diabetic patients measured by the Göthlin technic, it was found that the index of capillary fragility was above normal in practically all patients who had diabetic retinitis. It seems clear from our observation that diabetic retinopathy seldom occurs in patients who do not have some degree of increased fragility of the capillary walls.

Results in 56 Additional Diabetic Patients with Retinopathy

That there is a loss of the resistance of the capillary wall in diabetic persons is definite, and it is more evident when one studies selected diabetic patients with early or advanced retinopathy. The distinction between the two is of degree and stage of development. The proliferative type of retinitis often follows a period in which the typical central punctate hemorrhages of diabetic retinitis have been present for months or years. This picture constitutes the most serious menace, aside from arteriosclerosis, nephritis and hypertension, that persons with diabetes of long duration have faced.

In the hope of obtaining the new light on this subject that is so greatly needed, we studied an additional group of 56 selected patients with diabetic retinopathy. They were admitted to the hospital for routine check-up, regulation of diet and insulin or treatment of complications. The petechial index was increased in 47 (83.9 per cent) and borderline in 9 (16.1 per cent) and in no case was found to be normal. To this group of selected cases we add the 26 cases from the nonselected group listed in Table 1, making a total of 82 diabetic patients with retinopathy. The weakening of the capillary wall among these patients is definite, as shown by borderline petechial index in 9 cases and increased petechial index in 73.

Sex

Studying the effect of diabetes in the development of degenerative vascular diseases, Dry and Hines,[26] found enormously increased vulnerability among

women. Schneider et al.,[27] who studied the plasma proteins in diabetic retinitis, state that retinitis is more frequent in women. In their 31 cases, 26 patients (84 per cent) were women. Griffith and Lindauer, at the Scientific Exhibit of the American Medical Association in San Francisco in 1946, showed that there was no significant relation between capillary fragility and sex in their hypertensive patients. In our 82 diabetic patients with retinitis and increased capillary fragility, no significant predominancy was found among 44 women as compared with 38 men.

Blood Pressure

In these 82 diabetic patients with retinitis, 39 had normal blood pressures and 43 had pressures above 150 systolic, 90 diastolic.

Age of Patient and Duration of Diabetes

The age is an important factor in the consideration of capillary fragility. Moloney[24] found more or less abnormal capillary fragility in 33 of 55 normal infants, but this decreased resistance disappeared as the infant became older. Cutter,[23] in normal adults, showed that the fragility of the capillaries increased in direct proportion to age, and Paterson[5–7] states that the influence of age on the elasticity of capillaries may be an important factor in the causation of intimal hemorrhages. We must say, however, that the duration of diabetes appears to be more important. Rudy, Beaser and Seligman[4] reported that the incidence of increased fragility of the capillaries is great in the fifth and sixth decades and that in diabetic patients a greater incidence is observed at each age decade. It is interesting to observe that of the 82 diabetic subjects considered above 34 (41.4 per cent) were under forty years of age and that some were as young as twenty-one years; the duration of the diabetes, however, was generally more than ten years.

Of the entire group of 82 patients 48 were over forty years, with an average duration of eleven and a third years, and in the 34 patients younger than forty years of age, the average duration of diabetes was seventeen and three fourths years.

An abnormal condition of the capillaries may be an important factor in the production of certain vascular complications that occur in persons with diabetes of long duration. We consider it necessary to measure the capillary resistance in persons who have had diabetes for a long time. The importance of its early recognition is evident. This capillary condition will be the advent of the inevitable "period of exhaustion"[28] of the aging diabetic patient, who now lives longer not only with diabetes but also with degenerative diseases.

Results of Rutin Therapy

Rutin was administered to 70 patients, but only 20 have been followed adequately. The initial dose was 20 mg. three times a day, and in the 20 patients followed, the dosage was increased to 120 or 180 mg. daily after one or two months. No selection was made in this group of patients, whose ages were between twenty-three and sixty-one years, with a duration of diabetes from three to forty years. Twelve had blood pressures above 150 systolic, 90 diastolic. Eight had advanced retinitis proliferans, 6 had severe, and 6 had moderate diabetic retinopathy. To determine the effects of the therapy, capillary fragility was measured every month, and special attention was paid to the retinal picture, visual fields, blood pressure and evidences of sensitivity or toxicity from rutin.

Capillary Fragility

The petechial index became normal or borderline in 5 cases (25 per cent), remained positive but improved in 5 (25 per cent) and was not improved in 10 (50 per cent).

The following cases illustrate the effect of rutin therapy in diabetic patients with retinitis.

Case 24586. A 23-year-old woman with diabetes of 13 years' duration was examined in 1944 by Dr. W. P. Beetham, who found extensive retinitis proliferans with marked new capillary formation and sclerosis of the retinal veins, large hemorrhages and a few areas of cotton and waxy exudate. The visual fields were 20/200 on the right and 20/50 on the left. In April, 1946, the visual fields were 6/20 on the right and 6/15 on the left, and extensive retinitis proliferans involved a great portion of each fundus. The blood pressure was 118/86, and the capillary fragility index showed at least 300 petechiae. The patient started taking rutin in April, and the capillary fragility was regularly determined each month until April, 1947. The first reduction occurred 5 months after the beginning of medication, when the index fell to 182 petechiae. The reading was 56 in January, 1947, and was within the normal limits in April. Since July, 1946, she was definitely under the impression that her vision had improved, but as a matter of fact exactly the same visual acuity was obtained and no modification was seen in the retina. The blood pressure continued unaffected, and she had no rash or toxic reactions.

Case 21518. A 43-year-old man with diabetes of 4 years' duration developed typical central punctate hemorrhages, with waxy exudate in each fundus. The visual acuity was 6/7 in each eye; the blood pressure was 165/90, and the capillary fragility index was 42 in June, 1946. The patient received 60 mg. of rutin, and the dosage was increased to 120 mg. after 3 months. The capillary resistance became normal after 8 months. The retinal damage and visual field remained the same; the blood pressure was also unaffected.

In these cases the capillary fragility became normal with rutin treatment. In the first case, a young diabetic patient with long duration of the disease and with general vascular sclerosis, severe retinitis proliferans and a tremendous increase in fragility of the capillaries, after one year under rutin therapy the petechial index became normal. In the second patient, a man with diabetes of four years' duration, early diabetic retinitis and relatively moderate increase in capillary fragility, the petechial index was reduced progressively and reached the normal counting after eight months.

In the results reported by Griffith and Lindauer[2] in hypertensive subjects, the Göthlin test became

normal after four months of therapy, whereas in our diabetic patients with retinitis, only 25 per cent showed normal capillary resistance after eight months or more of therapy.

Retinitis

In no case was an improvement of the visual field or in the retinal picture seen, despite the fact that several patients were strongly convinced that rutin had improved their vision. The retinal picture was unchanged in 13 cases. Two patients had subsequent hemorrhages, and 2 had arterial thrombosis while taking rutin, whereas the hemorrhage was absorbed in 3.

In the patients who had new hemorrhages, the Göthlin test remained increased, and in some cases a rise in the index was seen with the new hemorrhages. A good example is provided by the following case:

CASE 17242. A 56-year-old man with diabetes of 23 years' duration had hypertension and bilateral diabetic retinopathy; typical punctate hemorrhages were present with vitreous opacities in each eye. The visual acuity was 20/70 on the right and 20/200 on the left, and the capillary fragility index in June, 1946, showed 95 petechiae. For 5 months he was taking rutin daily with progressive reduction of the petechial index, and after 8 months of medication new small hemorrhages developed in the left eye, with a new rise in the capillary fragility. The rutin dosage was increased to 120 and 180 mg., followed by marked reduction in capillary fragility, the petechial index actually dropping to normal. This patient was also under the impression that his vision had improved. However, the visual acuity remained exactly the same.

Another example is provided by Case 27954, in a forty-five-year-old man with diabetes of fifteen years' duration and with diabetic retinopathy and extensive vitreous hemorrhages without ocular hypertonus, who had visual acuity of 20/20 in the right eye and in the left merely perceived a flashlight. The capillary fragility was 24 in October, 1946, and remained abnormally high, with the appearance of subsequent new hemorrhages.

Miscellaneous

Following these 20 diabetic patients under rutin over a period varying from three months to a year, we have observed that the blood pressure in the entire group was unaffected, and no evidences of toxicity or sensitivity to rutin were seen.

Capillary resistance is definitely low in practically all persons with diabetic retinitis. This abnormality tends to decrease while rutin is being taken and the course of the retinitis is not altered as it was hoped. We should say, however, that rutin was given in the main to patients who already had advanced disease. Thus, the importance of the early recognition of this inevitable advent of capillary damage among patients with diabetes of long duration is evident.

We suggest the possibility that this lack of resistance of capillary wall related to retinitis and hypertension is also related to the degenerative complications — arteriosclerosis and the nephrotic syndrome — that constitute a specter in the prolonged life of the young diabetic patient.

SUMMARY

The literature on capillary fragility in relation to diabetic retinitis is reviewed.

Measurements of capillary fragility by the petechial index of Göthlin were done in a total of 156 diabetic patients. Forty per cent of 100 unselected diabetic patients showed an increased capillary fragility. This abnormality was found in practically all patients with diabetic retinitis, whether or not hypertension was present. In 11 cases hypertension was present with increased capillary fragility, but no retinal damage was observed.

In 56 selected cases with retinitis no patients showed a normal petechial index. The petechial index was increased in 47 (83.9 per cent) and borderline in 9 (16.1 per cent).

The incidence of increased capillary fragility was related to the duration of the diabetes more clearly than to the age of the patient; 41.4 per cent of 82 patients with retinitis were under forty years of age, and increased capillary fragility was observed as early as the age of twenty-one years, but with long duration of diabetes.

Rutin was administered to 70 patients with retinitis and increased capillary fragility. The initial dose was 20 mg. three times a day, and this was increased to 40 or 60 mg. three times a day in 20 cases. (A dosage of 300 to 400 mg. daily may be used.)

Increased capillary fragility can be brought to normal with the use of rutin in sufficient dosage, although no patient with retinitis was improved. Increased capillary fragility occurs in diabetic patients as an early evidence of generalized arterial disease and is closely correlated with the development of retinitis and later nephritis.

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FATAL INTESTINAL OBSTRUCTION FOLLOWING INJECTION TREATMENT OF AN INGUINAL HERNIA

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THE injection treatment of hernia is now so little practiced in regular surgical circles in New England that its results, favorable or unfavorable, are rarely observed. This report deals with a patient in whom a complete obstruction of the small intestine was attributable to the inflammatory reaction and adhesions produced by the injection treatment of an inguinal hernia.

CASE REPORT

H. J., a 57-year-old man, was admitted to the Burbank Hospital, Fitchburg, Massachusetts, on June 5, 1946, complaining of abdominal distention and constipation of 2 days' duration. This patient had had a reducible right inguinal hernia for several years and was currently receiving a series of injection treatments in a nearby town. He wore a truss in the usual way during the course of treatment. The last injection had been given on the morning of June 3. In the afternoon the patient began to feel ill, but had no pain. The abdomen gradually became distended; he lost his appetite, passed no gas and became constipated. That night his wife gave him a dose of castor oil, with no fecal results, and the distention increased. He had no nausea or vomiting but when first seen by his physician 2 days after the onset was complaining of moderately intense cramplike pains in the epigastrium.

Physical examination showed the patient to be dehydrated and somewhat toxic. The cardiovascular system seemed normal, and the lungs were clear. The abdomen was greatly distended and tympanitic throughout. No masses could be felt, and there was no localized tenderness. The right inguinal hernia was of medium size and entirely reducible.

The temperature was 98°F., and the pulse 88. The blood pressure was 150/100.

The urine was concentrated with a specific gravity of 1.026 and gave a + test for albumin but was otherwise normal. Examination of the blood disclosed a red-cell count of 4,910,000, with a hemoglobin of 98 per cent (Sahli), and a white-cell count of 5000, with 65 per cent neutrophils and 35 per cent lymphocytes. The blood nonprotein nitrogen was 32 mg. per 100 cc. An x-ray film of the abdomen showed several greatly dilated loops with the typical step-ladder pattern of obstruction of the small intestine.

Attempts were made to pass a Miller–Abbott tube, but after 24 hours the tube had not passed through the pylorus even under fluoroscopic manipulation. During the first 2 days in the hospital, the temperature remained nearly normal; the pulse ranged between 80 and 90, and repeated white-cell counts were not greatly elevated. The distention continued, however, and enemas in the hospital produced only a very small amount of fecal and gas return. At the end of 2 days he began to have fecal vomiting and fecal drainage from the Miller–Abbott tube, which was then lying in the stomach.

Two days after admission, when the patient was first seen by the author, the findings were essentially as noted above. The patient was only slightly dehydrated; he appeared somewhat toxic. The abdomen was diffusely and markedly distended and tympanitic. Individual loops of bowel could not be outlined, perhaps because of the rather obese abdominal wall. The only area of audible peristalsis was adjacent to the right flank. There was no abdominal spasm and no very definite tenderness. The right inguinal hernia was entirely reducible and also nontender. The hernia protruded again spontaneously when the finger was withdrawn from the external ring, with the patient recumbent and without cough or straining. A provisional diagnosis of obstruction of the small intestine, possibly due to the adhesions caused by the injection treatments of the hernia, was made.

An exploratory laparotomy was performed through a right paramedian incision. Clear, straw-colored fluid poured from the peritoneal cavity, and loops of greatly dilated and congested small bowel, measuring as much as 8.7 cm. in diameter in some places, presented in the wound. This dilatation of the intestine extended proximally to the ligament of Treitz and distally to a point in the lower ileum about 30 cm. above the ileocecal valve. At this point the small bowel was adherent to the parietal peritoneum of the right internal inguinal ring margin by several broad adhesions, which also tended to force a knuckle of bowel distal to this point into the inguinal canal. These adhesions were fresh and freed without difficulty. Some fibrinous exudate was also observed on the bowel in this area. These findings suggested that the whole process was of not more than a few weeks' duration. The bowel appeared perfectly viable. The abdomen was then closed without further procedure and without drainage. No attempt was made to repair the hernia itself, since it was believed that it would be unwise to prolong the operation further. The patient was in good condition at that time, however, with a systolic blood pressure of 120 and a pulse of 80. There was some excess of tracheobronchial secretions, but this cleared in the Trendelenburg position and the breathing then seemed satisfactory. The patient returned to the ward in good condition, but expired suddenly and with almost no warning while still under anesthesia, almost 2 hours later. Permission for autopsy could not be obtained.

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Discussion

As pointed out by Maier[1] in a recent report the treatment of hernia by the injection of sclerosing or irritating solutions evoked a great deal of enthusiasm in this country between ten and fifteen years ago. Its protagonists claimed excellent results with a minimum of complications resulting from the treatment itself. Watson,[2] for example, in the second edition of his textbook on hernia published in 1938, stated that he had performed over five thousand injections on 300 patients with hernia, with 95 per cent cures for small indirect inguinal hernias and between 80 and 90 per cent cures for larger or complicated hernias; similar remarkably good results were noted in several series totaling thousands of cases collected by him from the literature. One is impressed, however, by a lack of follow-up statistics based on acceptable time intervals such as one, two and three years in these reports. Watson claimed no serious complications from injection treatment in his own hands and no case of intestinal obstruction at the time of his report.

In 1937 Burdick and Coley[3] reported from the Hospital for Ruptured and Crippled in New York City their findings in a carefully controlled series of 92 cases of hernias treated by injections in an effort to evaluate accurately the place of this treatment. Although a high percentage enjoyed temporary relief of the hernias, these patients continued to wear trusses, and not 1 case was actually cured at the end of a year. Maier[1] reports from the same hospital on a series of 18 operations performed after previous injection treatments. He found marked scarring and atrophy of muscles and obliteration of normal tissue planes as a result of the sclerosing injections, which made the dissection and satisfactory repair very difficult. In 1 of these cases, obstruction of the small intestine due to incarceration of the bowel in the inguinal canal was encountered. Maier mentions several other cases of strangulated hernia caused by the unyielding "cartilaginous" internal rings produced by the injections. Rice,[4] an enthusiast ten years ago, now finds only a "narrow field of usefulness (for injection treatment) in slender individuals." It also seems significant that no articles favoring injection treatment have been published from responsible surgical clinics in over five years.

Summary

A case in which recent intraperitoneal adhesions resulting from the injection treatment of an inguinal hernia caused complete simple obstruction of the small intestine is presented in detail. This appears to be a rare complication of the injection treatment of hernia but should be added to a significant list of complications and sequelae that have been reported in the past.

Fortunately, interest in the injection treatment seems to be waning with the realization that this method cannot be depended on for cure of hernia in general.

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THE INCIDENCE OF MULTIPLE LESIONS IN PRIMARY SYPHILIS

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CHARLESTON, WEST VIRGINIA

ONE of the most popular misconceptions of the medical profession is that the primary lesion of syphilis is always single. In fact, many physicians have been known to eliminate syphilis as a part of the differential diagnosis because the genital lesions were multiple, not single. In our medical-school experience and that of our immediate acquaintances of the medical profession the impression was given that multiple primary lesions in syphilis are rare (in the dozen or so medical schools attended). Medical students and general practitioners can hardly be blamed, since authoritative authors such as Stokes et al.,[1] Sutton and Sutton[2] and Kampmeier[3] declare that multiple chancres are infrequently seen. Andrews[4] and Ormsby and Montgomery[5] mention that chancres are usually single but are frequently multiple.

The limited experience of general practitioners makes them utterly dependent upon these usual sources of knowledge concerning syphilis. Three out of five standard reference books give the impression that multiple chancres border on rarity.

One of us (I.W.K.), while reviewing his medical-school syphilology notes, experienced this impression. As a result, it was decided to determine what the actual figures were at the Kanawha Valley Medical Center, since it was the opinion that multiple primary lesions were not infrequent.

At this clinic we find that multiple lesions are not rare — in fact they are almost as common as single lesions, being approximately 40 per cent of the entire group of cases diagnosed as primary syphilis in 1946. In the literature only two other series of cases were found: Klauder's[6] in 1918 (24 per cent multiple lesions in 200 cases) and Driver's[7] in 1922 (38 per cent in 203 cases). The latter series agrees very closely with our own experience.

In an effort to determine whether these multiple lesions were definitely due to secondary syphilis, we listed separately all untreated, seronegative, dark-field-positive cases. This was done in accordance with the general assumption that more than 98 per cent of all cases of secondary syphilis have positive serologic tests. Thus, we have an unselected series of cases that were clinically primary syphilis and a selected series of cases that were still in the seronegative phase. To our amazement an even greater percentage of patients in the latter group had multiple lesions.

In the selection of these cases, penicillin in a small number of doses was not considered as treatment, whereas arsenicals or bismuth, or both, was considered treatment. The Kahn quantitative serologic test for syphilis, as done by the West Virginia State Hygienic Laboratory, was selected as the index of seronegativity or seropositivity, thereby using a common standard and eliminating various sensitivities — Kanawha Valley Medical Center Laboratory employs the Kahn standard test and Mazzini procedure; in the West Virginia State Laboratory, Hinton, Kolmer and Kahn quantitative tests are done routinely on all admissions.

There was no known bias of the examiners toward single or multiple lesions. At the time the compilation of figures was begun (March, 1947) four of the seven examiners had left this facility, and no such compilation had been anticipated before their departures. Most of the diagnoses were made by five of the seven examiners, and over half by two of them. The period covered was January 1 to December 31, 1946, inclusive.

At Kanawha Valley Medical Center 2023 patients with primary and secondary syphilis, 742 with early latent syphilis and 718 in other stages were admitted. In the unselected cases of primary syphilis the chancres were single in 378 (58 per cent), multiple in 251 (38.5 per cent) and indeterminate‡ in 23 (3.5 per cent). In the selected seronegative cases of primary syphilis the lesions were single in 107 (56.3 per cent), multiple in 82 (43.2 per cent) and indeterminate in 1 (0.5 per cent).

In the untreated seronegative primary cases, there were reinfections in 3, a monorecidive relapse in 1 and an extragenital lesion (breast of female patient) in 1. In the entire series of primary cases there were reinfections (Stokes criteria were not used by the examiners) in 24, monorecidive relapses in 16 and extragenital lesions in 10. Of the extragenital lesions observed in this series, only in 1 case were they multiple — so-called "kissing lesions" of the lips. Many extragenital primary lesions were observed, but the majority of patients were admitted in the secondary stage, presumably because of the unfamiliarity of the general practitioners with extragenital lesions and no suspicion of syphilis until a generalized rash appeared.

The oldest patient with primary syphilis was a 75-year-old man, and the youngest a boy of nine. Table 1 compares the sex incidence in selected and unselected cases. As noted many times before, the diagnosis of primary syphilis is made more frequently in male than in female patients. At this center 51.8 per cent of all persons seen (slightly more

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‡"Indeterminate" signifies that the examiner was unable to determine the number of lesions (usually because of phimosis) or neglected to note the number.

than half) were male patients, but in the unselected series of primary cases 87.3 per cent were male and 12.7 per cent were female patients — almost seven times as many males as females — and in the selected series the male preponderance was even greater: 93.2 per cent males to 6.8 per cent females, or almost fourteen times as many (Tables 2 and 3).

TABLE 1. *Sex Incidence in Selected and Unselected Cases of Primary Syphilis.*

SOURCE OF DATA	MALE PATIENTS %	FEMALE PATIENTS %
All patients	51.8	48.2
Unselected series	87.3	12.7
Selected cases	93.2	6.8

TABLE 2. *Sex Incidence in Cases Diagnosed as Primary Syphilis.*

SOURCE OF DATA	MALE PATIENTS		FEMALE PATIENTS	
	NO.	PERCENTAGE	NO.	PERCENTAGE
Entire series	569	87.3	83	12.7
Patients with multiple lesions	219	87.3	32	12.7
Patients with single lesions	327	86.5	51	13.5
Patients with indeterminate lesions	23	100.0	0	0.0

Thus, in our series it seems not only that more males seek treatment in the primary stage but also that in the earliest stage of diagnosis of syphilis (the seronegative, dark-field-positive, primary stage) the preponderance in the male is even greater.

TABLE 3. *Sex Incidence in Selected Cases Diagnosed as Primary Syphilis.*

SOURCE OF DATA	MALE PATIENTS		FEMALE PATIENTS	
	NO.	PERCENTAGE	NO.	PERCENTAGE
Entire series	177	93.2	13	6.8
Patients with multiple lesions	77	93.9	5	6.1
Patients with single lesions	99	92.5	8	7.5
Patients with indeterminate lesions	1	100.0	0	0.0

It is interesting that despite the wide variance of numbers of males and females, the percentage of multiple lesions is consistent in both series. In the unselected series 12.7 per cent were females, and 12.7 per cent of those with multiple lesions and 13.5 per cent of those with single lesions were females. In the selected series 6.8 per cent were females, and 6.1 per cent of those with multiple lesions and 7.5 per cent with single lesions were females. Thus, the percentages were of the same orders in both series, and there seems to be no tendency for females or males to have single or multiple lesions more frequently than those of the other sex.

CONCLUSIONS

Multiple lesions are common in primary syphilis — 38.5 per cent of 652 primary diagnoses being multiple.

In 190 seronegative dark-field-positive untreated cases of primary syphilis 43.2 per cent of patients had multiple lesions.

Persons with multiple primary lesions tend to come for treatment earlier than those with single lesions.

Patients with extragenital primary lesions are seldom treated in the seronegative state.

Primary syphilis is no respecter of age.

The diagnosis in the primary stage of syphilis is made much more frequently in male than in female patients — 87.3 per cent and 12.7 per cent respectively.

Male patients seek treatment earlier than females in primary syphilis (93.2 per cent of the former and 6.8 per cent of the latter in the selected "early" series).

There is no recognized tendency for one sex to have multiple primary lesions more frequently than the other.

Extragenital primary lesions are more frequently single than genital primary lesions.

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MEDICAL PROGRESS

DIABETES

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THE following subjects are considered in this progress report on diabetes: statistics; diabetic acidosis and coma; the hyperglycemic action of highly purified alkaline phosphatase; convulsive states in diabetes; electrocardiographic changes; arteriosclerosis; pregnancy in diabetes; metabolism of carbohydrate and fat; the diabetes section of the United States Public Health Service; new rapid blood sugar tests; and alloxan diabetes.

STATISTICS

Variations in diabetes mortality in different countries and even in the different states of the United States are so glaring as to arrest attention and demand explanation. Such a diversity of statistical data can be explained partly by different methods of recording deaths, accessibility to medical supervision and availability for statistical enumeration. In this neighborhood the fallacy of estimating the true mortality and much more the computation of the true incidence of diabetes from reports of fatal cases has again been shown by a comparison of the death certificates in a series of deaths of 1000 known diabetic patients: only 63.2 were reported as diabetic according to the joint causes of death.[1] The remainder escaped enumeration because of the absence of the word "diabetes" on the certificate, its mention as a secondary cause of death or another disease given priority. Therefore, the Oxford, Massachusetts, survey in which urine and blood specimens of the inhabitants were examined, conducted by Wilkerson and Krall,[2] of the United States Public Health Service, is a major contribution to knowledge of the incidence of diabetes.

The town of Oxford, Massachusetts, has 4983 inhabitants and is diabetes conscious because a children's diabetes camp has been in operation there for seventeen years and these hundred children are an every-day sight on the streets, in bathing or at church. The inhabitants of the town, therefore, were co-operative in the survey, and 3516, or 70.6 per cent, submitted to tests of the blood and urine. For the 40 known diabetic patients in the community prior to the survey 30 persons with unrecognized diabetes were discovered, and if all residents had been examined, the implication is that for each *known* there was an *unknown* case of diabetes. Oxford is a representative community, the age composition of the population closely paralleling that of the country as a whole. The incidence of diabetes in the Oxford Survey based on the total population was 0.8 per cent for known cases and 0.6 per cent for newly discovered cases, or a total incidence of 1.4 per cent for the 4983 inhabitants. The ages of the newly discovered diabetic persons varied between sixteen and ninety-three years, with a median age of fifty-five years, those from forty-five to sixty-four years of age constituting nearly half the cases and more than half the new cases. In the cases in the age decades tested, from forty-five years on, the percentages of diabetic patients found were surprisingly high (Table 1). Thus, between forty-five and fifty-four it was 4.6 per cent, between fifty-five and sixty-four it was 5.1 per cent, and between sixty-five and seventy-four it was 7.3 per cent, rising above the age of seventy-five to 13.0 per cent. If these figures were substantiated by similar figures in larger groups, diabetes would be even a greater geriatric problem than already anticipated.

TABLE 1. *Prevalence of Diabetes in Oxford, Massachusetts.*

AGE INTERVAL	TOTAL NO. OF PERSONS TESTED	TOTAL NO. OF DIABETIC PERSONS
yr.		
Under 15	931	0
15 to 24	521	2
25 to 34	606	2
35 to 44	489	9
45 to 54	411	19
55 to 64	295	15
65 to 74	192	14
75 and over	69	9
Unknown	2	—

The sex distribution among the 70 cases revealed 31 men and 39 women. There was a high prevalence of the disease among the French or those of French-Canadian descent. A family history of diabetes was reported by 38.6 per cent of the diabetic and by 18.2 of the nondiabetic persons. Overweight was the rule. The survey showed the unreliability of the fasting blood sugar level as a means of diagnosing early

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diabetes and emphasized the necessity of using both blood and urine tests for diagnosis. If urinalysis alone had been employed 8 cases would have escaped diagnosis, and if only a blood specimen had been taken 6 cases would have escaped detection.

For the group tested in Oxford the screening level for hyperglycemia was 160 mg. per 100 cc. for venous blood and 190 mg. per 100 cc. for capillary blood. Persons with a blood sugar below the screening level and no glycosuria were notified that the tests revealed no laboratory evidence of diabetes. If glycosuria with or without a blood sugar above the screening level was encountered, a further test of urine and blood was given. Dextrose tolerance tests were performed if previous tests of blood and urine were not in accord or borderline or if there was persistent hyperglycemia without glycosuria or vice versa. The details are given in the original article, which is replete with valuable data, such as those concerning the known diabetic persons tested between the ages of fifteen and twenty-four. This is the only group in which a large enough number of both venous and capillary specimens were examined to permit direct comparison, which demonstrated a difference of 20 mg. between average venous and capillary blood sugar level.

The ratio of cases of diabetes to the portion of population tested revealed that there were 40 diabetic persons in Oxford under treatment and 30 more cases of the disease discovered, which represents an

TABLE 2. *Death Rates from Diabetes Mellitus, 1940 (Adapted from Marks[5]).*

GEOGRAPHIC DIVISION	TOTAL DEATH RATE		DEATH RATE FOR WHITES		DEATH RATE FOR NONWHITES	
	ADJUSTED*	CRUDE	ADJUSTED*	CRUDE	ADJUSTED*	CRUDE
	per 100,000	*per 100,000*	*per 100,000*	*per 100,000*	*per 100,000*	*per 100,000*
United States	26.6	26.6	26.7	27.6	23.2	17.9
New England						
Maine	25.3	32.1	25.3	32.1	†	†
New Hampshire	28.1	37.0	28.1	37.1	0	0
Vermont	27.0	33.7	27.0	33.7	0	0
Massachusetts	29.8	35.7	29.8	35.8	30.1	30.4
Rhode Island	35.4	38.8	35.0	38.5	†	†
Connecticut	32.8	35.8	32.6	35.9	40.8	32.5
Middle Atlantic						
New York	39.0	40.6	38.8	41.2	39.7	27.9
New Jersey	35.6	36.4	34.9	36.2	51.0	39.7
Pennsylvania	35.9	36.3	35.4	36.3	46.5	36.3
East North Central						
Ohio	28.1	31.3	27.6	31.2	39.8	33.4
Indiana	24.2	28.1	23.8	27.9	35.7	33.5
Illinois	32.0	34.1	31.5	34.1	38.9	34.3
Michigan	27.9	26.7	27.7	26.8	32.0	22.6
Wisconsin	26.0	28.4	25.9	28.4	†	†
West North Central						
Minnesota	24.5	26.8	24.4	26.8	†	†
Iowa	23.1	28.4	22.9	28.3	†	†
Missouri	21.6	25.3	21.4	25.5	23.2	22.8
North Dakota	28.7	26.6	28.6	26.6	†	†
South Dakota	23.0	23.2	22.8	23.3	†	†
Nebraska	24.7	28.1	24.8	28.2	†	†
Kansas	21.7	26.0	21.5	25.9	27.3	30.1
South Atlantic						
Delaware	27.6	30.0	26.2	29.5	37.1	33.4
Maryland	31.5	31.2	32.3	33.5	24.4	19.5
District of Columbia	34.9	33.5	33.5	35.2	38.0	29.1
Virginia	23.5	20.1	22.5	19.9	25.9	20.7
West Virginia	21.6	17.4	21.0	17.0	32.6	22.9
North Carolina	20.0	14.2	20.2	14.8	19.1	12.6
South Carolina	18.7	12.6	20.8	14.4	15.7	10.2
Georgia	15.5	12.2	16.8	13.8	12.6	9.1
Florida	20.1	19.6	19.6	21.2	19.7	15.3
East South Central						
Kentucky	16.9	15.7	16.5	15.2	21.2	21.9
Tennessee	16.4	14.2	14.9	13.0	22.7	20.0
Alabama	15.9	12.2	16.0	12.4	15.6	11.7
Mississippi	16.9	13.4	17.8	14.9	16.1	11.8
West South Central						
Arkansas	12.4	10.5	12.9	11.1	10.3	8.5
Louisiana	22.4	17.5	24.2	19.2	18.8	14.4
Oklahoma	16.0	14.4	15.7	14.3	19.0	15.5
Texas	17.2	14.4	16.9	14.3	18.6	14.9
Mountain						
Montana	19.3	19.3	19.7	19.3	†	†
Idaho	19.0	17.5	19.3	17.7	0	0
Wyoming	20.1	16.4	19.6	15.8	†	†
Colorado	16.4	17.8	16.5	17.9	†	†
New Mexico	12.1	8.3	12.7	8.7	†	†
Arizona	14.3	11.0	14.1	11.0	†	†
Utah	23.4	19.4	23.7	19.7	0	0
Nevada	21.0	20.9	20.7	20.2	†	†
Pacific						
Washington	21.9	26.1	21.8	26.1	†	†
Oregon	21.6	25.9	21.6	25.9	†	†
California	21.2	24.7	21.1	25.0	22.7	18.0

*Adjusted on basis of age distribution of the total population of the United States enumerated in 1940.
†Less than 10 deaths.

incidence of 0.8 per cent known and 0.6 per cent newly discovered cases, or a total incidence of 1.4 per cent for the 4983 inhabitants. Since 29.4 per cent of the townspeople were not reached by the testing program, it is estimated that the number of previously undiscovered cases of diabetes might have risen to 47 had all the townspeople been tested. The 40 known cases in addition to these 47 estimated cases would be equivalent to 1.7 per cent of the population of the town.

The early discovery of diabetes may be considered a form of preventive medicine, because it is generally agreed that the case detected early does the best. Statistics of diabetes discovered by life-insurance examination and of the disease in the medical profession and in the Army, as well as the opinions of doctors intimately concerned with treatment, attest this idea.

This survey is of great importance. It has set a new standard for estimates of the prevalence of diabetes. If the data obtained are duplicated and hold for the country as a whole, the implication would be that instead of 1,000,000 diabetic persons in the United States there are actually 2,000,000. The million *unknown* cases would on the whole be the ones most amenable to treatment, because the majority would be the mild, symptomless cases and those of recent onset, by all standards presenting the best prognosis, but at the same time probably of a lower income group, thus necessitating special provisions for treatment. Moreover they constitute the group *par excellence* for possible obtaining of life insurance and thus may arouse the interest of life-insurance companies — greatly to the advantage of the diabetes situation. On the other hand, one must remember that a small percentage of unrecognized diabetic cases are severe, because the knowledge of the diabetes is first disclosed after entrance to the hospital in diabetic coma. Thus, of 10 patients representing nine decades of life, shown by Joslin in Indianapolis in late 1946, none knew they had the disease until advised of the fact on their recovery from acidosis in the Indianapolis City Hospital. The patients were in the low-income group.

This survey has substantiated the notable and unexpected incidence of diabetes as found among Selective Service registrants by Blotner[3] and by Gates[4] in an industrial establishment.

In a comprehensive discussion of recent studies on diabetes and diabetic patients, Herbert H. Marks,[5] of the Statistical Department of the Metropolitan Life Insurance Company, arrives at the conclusion that the number of *known* cases in the United States is in the neighborhood of 700,000. In any comparison of Mr. Marks's estimate with other estimates, one should bear in mind that figures larger than this include some unknown as well as known cases. He believes that there are 55,000 new cases annually, thus raising his estimate by 5000 since 1946.[6] Approximately 4,125,000, or 2.9 per cent of the population (2.1 per cent of the males and 3.8 per cent of the females), he considers, will become diabetic before they die. The highest rates are in the urbanized industrial states in the northeast section of the country and the lowest in the southern states and the southwest. Where the Negro population is urbanized and has access to abundant medical and health service, their diabetic death rates are high. For the country as a whole, white and Negro age-adjusted death rates were more than 50 per cent higher in cities than in rural areas; this was true — and even by more than 100 per cent — for the nonwhite population. In the article by Mr. Marks is a table for each state in the country, showing crude and age-adjusted diabetes death rates per 100,000 whites and nonwhites separately for 1940 (Table 2).

TABLE 3. *Death Rates from Diabetes Mellitus in Various Countries, 1938.**

COUNTRY	DEATH RATE *per 100,000*	COUNTRY	DEATH RATE *per 100,000*
United States	23.9	Belgium	19.7†
Canada	13.8	France	10.1§
Argentina	7.0‡	Italy	10.5
Uruguay	5.8†	Spain	9.4¶
Chile	4.6†	Portugal	6.2†
England and Wales	11.5	Lithuania	3.7†
Scotland	17.2	Esthonia	3.0‡
Northern Ireland	12.9	Czechoslovakia	12.3†
Irish Free State	9.2	Hungary	6.1†
Norway	9.0	Bulgaria	7.8‡
Sweden	10.8	Roumania	3.0‡
Denmark	20.4	Greece	4.9
Finland	8.1	Australia	17.7
Germany	19.3‡	New Zealand	18.8
Austria	12.2†	Union of South Africa	13.5
Switzerland	15.4‡	Japan	4.2
Netherlands	14.5		

*Adapted from Marks.[5]
†1937.
‡1936.
§1934.
¶1935.

To Mr. Marks we are also indebted for Table 3, which gives the death rates per 100,000 for diabetes mellitus in various countries of the world for the year 1938. The high rates for the United States and Denmark are significant. It is difficult to understand why England and Wales, Norway, Sweden, Finland and the Netherlands have such low mortalities — 14.0 per 100,000, provisional for 1939 — compared with the neighboring countries of Denmark and Belgium.

The experience of the Metropolitan Life Insurance Company since 1911 shows a steady increase in the crude death rates from diabetes to a maximum in 1940. Since then, the rate has fallen rather rapidly, with the 1945 rate the lowest since 1938. A notable feature of the trend in mortality is the decline recorded during the recent war years. The experience of England shows that "at the low point in 1945, the English death rate from diabetes was more than 25 per cent under the peak of 1940, and more than 20 per cent under the average for 1935–1938."

It would appear that a significant part of the reduction in diabetes mortality recorded in the two wars is genuine and that restrictions on food supply are a factor in this trend. The enforced reduction in food intake tends to ameliorate the condition of many diabetics and also helps to prevent or postpone the onset of the disease in susceptible individuals. In this country at least, the favorable trend in diabetes during World War II reflects also the absence of serious respiratory epidemics during the entire war period, as well as the success of chemotherapy. This has proved a boon to diabetics not only in combating pneumonia and other infections, but also in the successful management of surgical complications of diabetes. On the other hand, the decline in the diabetes death rate is spurious to some extent in that, with the wartime disruption of medical practices, the reporting of causes of death probably suffered in quality.

The most notable feature of the wartime mortality experience for diabetes is the considerable decline in the death rates in late middle life and old age. The rates in 1944 and 1945 were the lowest in years. However, the recent improvement at the older ages was sufficient to wipe out only a fraction of the long-term increase in the death rates from the disease. Consequently, at ages 65 to 74, the rate in 1941–1945 among males was 34 per cent higher than in the preinsulin years, 1920–1922, and among females, it was 81 per cent higher than in 1920–1922.

Statistics on the incidence of diabetes in Mainfranken in 1944 were recorded by Oberdisse and Nagel[7] as 1.90 per 1000 population as compared with 2.13 for Bavaria and 2.29 for the whole of Germany. Lombard[1] computed a mortality rate of 5 per 1000 as representing the situation in 1947 in Massachusetts.

A series of patients admitted to the Central Hospital, Boras, Sweden, between 1932 and 1941 have been analyzed and reported by Dahlberg and Grill.[8] At the conclusion of the period a follow-up study showed that 515 patients (66 per cent) were alive, 240 (30.8 per cent) dead and 24 (3.2 per cent) untraced, making a total of 779 cases. Female patients predominated — 55.8 per cent of the living and 60.7 per cent of the dead.

An attempt was made to compare the first five years, in which the calculated low-carbohydrate Petrén diet was employed, with the second five years, in which the normal diet was given, but the writers properly point out that the small number of cases and various extraneous factors enter into such a comparison. In the second five years the daily diet varied in carbohydrate between 296 and 369 gm., in protein between 91 and 151 gm., in fat between 94 and 120 gm., and in calories between 2605 and 3127 for individual days. It is evident that the percentage of patients admitted on account of diabetes was less in the second than in the first period, and, correspondingly, the percentage admitted on account of other diseases was greater in the second than in the first period. The fact that insulin was given to 52.5 per cent of patients admitted in the first five years, compared with 74.2 per cent in the second five years, must be considered in any evaluation of the two types of treatment. The cost of insulin purchased by the Central Hospital of Boras for patients treated in the Hospital was 2839 kroner for the first five years and 6421 kroner for the second five years. Hypoglycemia was present in 5 cases in the first period and in 28 in the second, also showing the greater use of insulin. The average stay was twenty-four days in the first group and twelve days in the second. Coma and pre-coma occurred nearly half less often in the second than in the first period, but here again the influence of insulin and not the diet alone must be taken into account.

Of the 240 deaths, cardiovascular disease accounted for 50 per cent, general and local infections for 16 per cent, and diabetic coma for 5 per cent. Of the 12 deaths from coma, 11 were in females, and the authors state "that these figures indicate a sex difference in resistance to ketone formation." On the other hand, one might compare the 28 deaths from diabetic coma in the Joslin group treated at the New England Deaconess Hospital during a similar period, of whom 8 were males and 20 were females, and the mortality 6 per cent among the males and 9 per cent among the females. The Boras cases, like the Joslin series, show an increasing mortality from coma when it occurs in older people. Their total mortality from diabetic coma in their follow-up was 5 per cent as compared with 3.1 per cent in a follow-up of 651 deaths in the Joslin group for January 1, 1944 to May 15, 1946. The diagnosis "diabetes," which was reported especially in older people, was 10 per cent, and that of tumors was 7 per cent, with 16 deaths from miscellaneous causes. The authors conclude that the probable mortality among diabetic persons is three times as great as that of the general population.

The year 1948 completes my fifty years of practice of medicine and active interest in diabetes. The results of treatment of the cases coming under my supervision and that of my associates under the auspices of the George F. Baker Clinic in Boston were recently published in the Statistical Bulletin of the Metropolitan Life Insurance Company.[9] All my cases, anonymously by number, have been summarized on cards, and the statistical studies have been carried out in the Statistical Bureau of the Metropolitan Life Insurance Company. For the preparation of these statistics 99 per cent of the patients treated since 1898 have been traced, largely as a result of the courtesy of the medical profession in responding to requests for information. The death rates (Table 4) and the increasing longevity of diabetic patients (Fig. 1) give ground for encouragement.

Both the table of mortality and the chart of life expectancy agree in showing that in each successive period of treatment for all ages there has been absolute uniformity in that the results have been steadily improving for each succeeding epoch. The following quotation is illustrative:

At the younger ages these reductions were nothing less than spectacular. Thus at age 10, the death rate in 1922–1925 was 84 per cent less than in the period 1914–1922.

Further sharp gains have been made at every age down to the present, and as before, these have been relatively greatest at the younger ages. Thus, even between 1929–1938 and 1939–1945, the most recent of the periods into which the data are divided for comparison, the death rate at age 10 showed a decline of 43 per cent, and at most ages under 45 the reduction between these two recent periods exceeded 30 per cent.

When the rates in the most recent years, 1939 to 1945, are compared with those prevailing before insulin, the revolution in the outlook for diabetics is even more sharply defined. At age 10, the recent rate is *99 per cent less* than in 1914–1922. Reductions of 95 per cent or more are found at all ages up to 30 and of 90 per cent to 95 per cent at ages 30 to 40. Even at age 60, the highest age shown in the table, the rate in 1939–1945 was 53 per cent less than in 1914–1922.

Figures for expectation of life of diabetics computed from the mortality rates observed among these patients of the George F. Baker Clinic likewise attest the very great improvement in the outlook for persons with the disease. The chart on page 7 shows the expectation of life at the selected ages of 10, 30, and 50 years, in successive periods before and since the discovery of insulin. Prior to 1914, the average 10-year-old diabetic child lived a little more than a year, and during 1914–1922 the expectation of life at age 10 was only a little higher — about 2½ years. The first years of insulin, 1922–1925, saw a gain of nearly 12 years, and marked increases have been recorded in every successive period. Even the most recent period, 1939–1945, shows a gain of a little more than 5 years in the expectation of life at this age over 1929–1938. Today, with an expectation of life of 45 years, the average diabetic child of 10 in this experience may expect to reach his 55th birthday.

Analysis of the causes of death among diabetics in this experience shows further what insulin and other advances in the treatment of diabetes have accomplished. Before insulin, diabetic coma snuffed out the lives of practically every diabetic child and of many diabetic adults. The death rate in recent years from this cause is 99 per cent less than in pre-insulin days. The mortality from gangrene, which was a frequent cause of death of diabetics in earlier years, has been reduced nearly 60 per cent. The mortality

TABLE 4. *Death Rates among Diabetic Patients in 1897–1945, according to Experience at George F. Baker Clinic.**

AGE	DEATH RATES†					
	1897–1913‡]	1914–1922‡	1922–1925§	1926–1928§	1929–1938§	1939–1945§
yr.	*per 100,000*	*per 100,000*	*per 100,000*	*per 100,000*	*per 100,000*	*per 100,000*
10	824.0	386.1	61.4	19.1	8.1	4.6
15	623.0	398.8	84.0	14.9	9.2	5.6
20	614.0	410.8	89.4	18.3	12.6	7.6
25	585.6	342.8	77.4	28.0	15.9	10.1
30	359.8	236.8	74.8	33.4	13.9	9.8
35	200.6	152.1	57.5	28.5	10.6	9.4
40	165.7	115.1	34.7	23.8	16.6	10.4
45	119.8	87.1	33.4	26.3	22.2	15.2
50	96.1	77.4	45.3	41.0	30.6	24.3
55	97.1	90.1	64.2	56.5	46.4	36.4
60	188.8	112.5	85.2	70.1	66.6	52.4

*Adapted from *Statistical Bulletin, Metropolitan Life Insurance Company.*[9]
†Excludes deaths within one week of first observation or hospital discharge.
‡Preinsulin era.
§Insulin era.

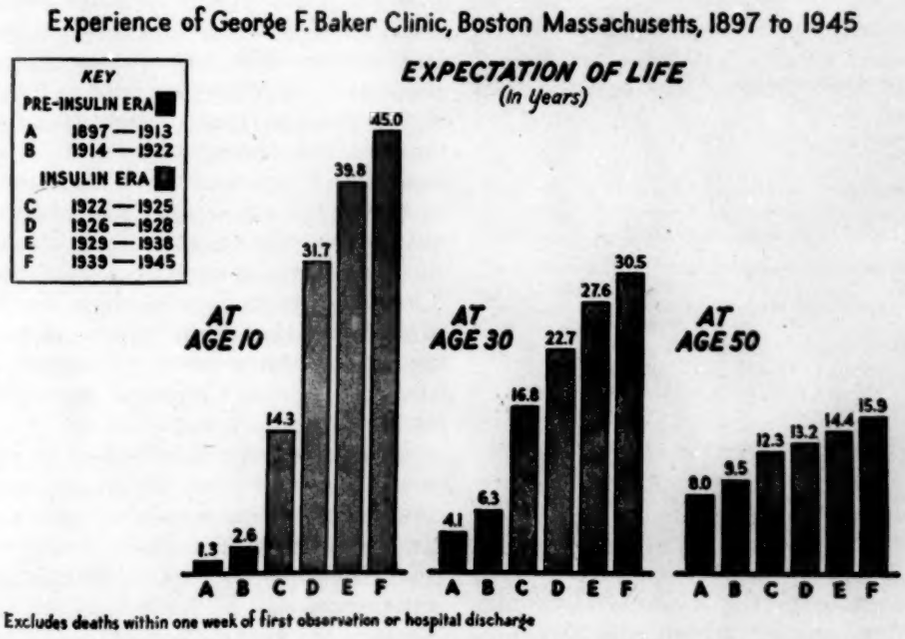

FIGURE 1. *Increasing Longevity of Diabetic Patients* (*Reproduced from* Statistical Bulletin, Metropolitan Life Insurance Company[9] *by Permission of the Publishers*).

from infections, to which diabetics are particularly susceptible and which in pre-insulin days were highly fatal, has likewise been cut radically: the death rate from pneumonia to one sixth of the pre-insulin rate, and from tuberculosis to one eighth.

The chief causes of death which show little or no reduction in mortality are the cardiovascular-renal diseases and cancer, but this is not surprising in view of the similar trends in the general population and in view of the increasing average age of the diabetic patients in this experience.

Despite the very satisfactory improvement in the prognosis for diabetics demonstrated by this experience, further substantial gains can be achieved. The length of life of patients in this experience is, at every age, still about one fourth less than that of the general population.

Berkson, Gage, and Wilder[10] have made life tables for diabetic patients based upon the experience of patients observed at the Mayo Clinic between 1923 and 1938 and traced, for the most part, through 1940. The authors included all patients diagnosed as diabetic except those who at the original observation also had a malignant neoplasm. Their series consists of 7408 patients, most of them residents of the middle West. Unlike most clinical series, male patients outnumbered female. The proportion of children was unusually small. In addition to the main group a separate analysis was made of cases free of "associated diseases"; this group numbered 992, or 13 per cent of the total. The authors compared the mortality experience among diabetic patients of the Mayo Clinic with that of white persons of the general population in 1930, the approximate mid-point of this experience.

Table 5 shows the death rates per 1000 by age in this experience by ten-year age groups. The death rates are at their lowest level at the childhood and early-adult ages, and rise sharply after the age of forty. The yearly death rate at all ages for the total experience adjusted to the age distribution of white persons in the general population in 1930 was 25.2 per 1000. This is approximately two and a half times the death rate for the white population of the country in 1930. For cases free of "associated diseases," the rate was 19.5, or nearly twice the figure for the general population. The rate for females was about 10 per cent less than that for males; in the general population in 1930 the difference was 16 per cent. The comparison with the general population is more favorable at the older than at the younger ages. At most ages under forty, the death rates among the diabetic persons were more than three times as high as the 1930 figure for the general population; between ages ten and twenty, they were more than seven times as high.

Figures on expectation of life computed from the mortality rates observed are shown in Table 6 and the corresponding figures for white persons in the general population in 1930. At age ten, the expectation of life for diabetic patients in the Mayo Clinic experience was 37.8 years as compared with 56.6 years in the general population. The figures decline steadily with age, as do those in the general population. At most ages, the figures for the diabetic patients were about a third less than those for the general population in 1930.

The results of this analysis conform to those reported for patients of the George F. Baker Clinic, although the figures are not strictly comparable, principally because of the difference in the periods

TABLE 5. *Annual Death Rates among Diabetic Patients of the Mayo Clinic (1923–1938, with Patients Traced to 1940).*

Age Interval	All Cases			Cases with No Associated Diseases		
	Person-years in interval	Deaths in interval	Annual death rate	Person-years in interval	Deaths in interval	Annual death rate
yr.			*per 1000*			*per 1000*
Under 10	479	4	8.4	297	3	10.1
10–19	1873	30	16.0	968	16	16.5
20–29	2531	27	10.7	1074	11	10.2
30–39	3839	70	18.2	1084	12	11.1
40–49	7248	177	24.4	1168	16	13.7
50–59	12944	496	38.3	1326	38	28.7
60–69	12717	927	72.9	1211	59	48.7
70–79	4668	557	119.3	336	45	133.9
80 and over	491	86	175.2	16	1	64.5
Totals	46790	2374	50.7	7480	201	26.9
Mean death rate, standardized*			25.2			19.5

*Standardized on the basis of age distribution of white persons in the United States, 1930.

TABLE 6. *Life Expectancy of Diabetic Patients of the Mayo Clinic Compared with that of the General Population by Sex and Age (1923–1938, with Patients Traced to 1940).*

Age	Life Expectancy* of Diabetic Patients of Mayo Clinic			Life Expectancy* of White Persons, United States, 1930
yr.	Both sexes	Males	Females	
10	37.8	37.4	38.3	56.6
20	33.6	32.3	35.3	47.1
30	26.8	25.3	28.6	38.6
40	21.3	20.1	22.8	30.2
50	15.6	14.9	16.3	22.3
60	10.5	10.4	10.6	15.3
70	7.2	7.0	7.3	9.5

*Expectancy for diabetic patients calculated by method of Reed and Merrell for constructing an abridged life table.

covered in the two experiences. The analysis of the George F. Baker Clinic records shows a steady increase in the longevity of diabetic persons since the discovery of insulin.

Diabetic Acidosis and Coma

The essential feature emphasized at the New England Deaconess Hospital and responsible for the improvement in mortality of its cases of coma during the last seven years is the attitude that every case of diabetic acidosis and coma is a grave emergency and that the patient needs intensive study, to determine the diagnosis and especially to determine the complications present, as well as an immediate effort to determine the amount of insulin needed and to give that dose as promptly as possible. Occasional, profoundly unconscious patients may need 500 to 1000 units, and if any less than this dose is given in the first few hours, delay occurs at a time when it is most dangerous. Those who adopt automatic rules by which a patient gets 50 units every thirty minutes may find in the occasional very severe case that in the first two or three hours only a comparatively small amount of insulin has been given and during that time the patient has lost ground.

The striking improvement in the mortality rate of profoundly unconscious patients at the Deaconess Hospital has been due to willingness to give 500 or 1000 units, or even more, in the first two hours of treatment when it is necessary. Thus, whereas 35 per cent of the profoundly unconscious patients died in the period before 1940, since 1940 only 10 per cent have died. Everyone knows that the mortality in the profoundly unconscious patient is higher than that in patients who are not yet completely unconscious. Thus, Nicholson and Branning[11] report a mortality of 64.6 per cent in 55 patients in coma who were profoundly unconscious. When they omitted from this series unconscious patients whose deaths were due to complications other than coma, they still had a mortality of 48.8 per cent. Another striking fact brought out in their article had to do with the use of sodium lactate. Thus, patients who received sodium lactate showed a mortality of 8.5 per cent for those twelve hours in coma, 66.6 per cent for those in coma from twelve to twenty-four hours and 50 per cent for those in coma for twenty-four hours. Patients treated without sodium lactate showed a mortality of 9.1 per cent for those twelve hours in coma, 22.2 per cent for those in coma twelve to twenty-four hours and 66.6 per cent for 3 patients in coma for twenty-four hours. Little advantage was obtained by the use of sodium lactate. They also described 2 cases of diabetic acidosis associated with a decrease in the serum potassium concentration, with recovery in 1.

Shock may occur with coronary occlusion, as in Case 24095 with a fall in the blood carbon dioxide to 20 vol. per cent but with no acetone bodies in the blood. Differential diagnosis is therefore important. This case might have been thought to be a death from diabetic coma if there had not been quantitative measurement of the acetone bodies in the blood, which showed less than 2 mg. total acetone bodies per 100 cc.

In the treatment for diabetic acidosis of 96 children, Hartmann and Erganian[12] made use of sodium lactate to raise the blood carbon dioxide. The method is summarized by the statement that insulin is immediately administered in amounts of 2 units per kilogram of body weight, and 30 cc. of sixth-molar sodium lactate solution per kilogram of body weight is given intravenously. At the same time 40 cc. of hypotonic Ringer's solution per kilogram and 30 cc. of sixth-molar sodium lactate per kilogram of body weight are given subcutaneously. Six hours later approximately 0.5 unit of insulin per kilogram is administered, and if necessary sixth-molar sodium lactate is given subcutaneously and plasma, concentrated albumin or whole blood as required. Five of the 96 children died, although acidosis was relieved before exitus.

(To be continued)

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 34121

PRESENTATION OF CASE

A sixty-six-year-old housewife entered the hospital with swelling of the right leg.

Two weeks prior to admission, following a day of standing at the election polls, swelling of the right leg appeared, with slight aching referred to the hip and lower back. A physician advised bed rest, which resulted in definite improvement during four days' rest, but upon arising the swelling and discomfort returned.

Physical examination revealed a comfortable patient with marked pitting edema of the right leg, extending to the thigh. The extremity was cyanotic and cool, with moderate venous distention and diminished arterial pulsations on that side. A small area of tenderness was found over the calf. Homans's sign was negative. There was also slight edema of the left lower leg. No other abnormal signs were observed.

Examination of the blood disclosed a red-cell count of 4,400,000, with a hemoglobin of 15 gm., and a white-cell count of 5900, with 69 per cent neutrophils, 22 per cent lymphocytes and 9 per cent monocytes. Urinalysis was negative, and the prothrombin time was normal. An x-ray film of the chest was normal.

Following admission heparin and dicumarol therapy were instituted, and the patient was maintained with a prothrombin time of 40 to 60 seconds (control, 18 seconds) for about two weeks, following which she was allowed up with a constricting dressing on the right leg. During this period the temperature occasionally reached 99°F., and she complained of vague pain in the upper lumbar area. An intravenous pyelogram showed the right kidney to be displaced to the right by a mass that extended 5 cm. to the right of the lumbar spine. A barium enema revealed an abnormality of contour having the appearance of extrinsic pressure just distal to the hepatic flexure, which was moderately displaced. A gastrointestinal series showed the duodenum to be quite definitely displaced, principally anteriorly, but also slightly to the left. A diverticulum extended from the second portion of the duodenum. No other contributory findings were discovered by x-ray examination.

About four weeks following admission, an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. HORATIO A. ROGERS: I am sure that I should see the x-ray films before I go any farther.

DR. STANLEY M. WYMAN: The lung fields appear clear. The heart shadow is not remarkable. There are no visible mediastinal or hilar masses. The film of the abdomen shows dye in the right urinary passages and a smooth, somewhat spindle-shaped mass extending to the right of the spine, compressing the upper pole of the kidney on the right and displacing it laterally. This is well seen in the oblique view. There is no unusual area of calcification. There are no other visible masses in the abdomen. The liver and spleen do not appear remarkable. The displacement of the colon is seen here, with the suggestion of an extrinsic pressure defect in the proximal transverse colon. The duodenum is displaced considerably anteriorly in this film, but one cannot outline the mass well.

DR. ROGERS: The finding of edema of the leg without previous symptoms is in favor of a local rather than a systemic cause of swelling. Direct pressure or venous thrombosis could account for the swelling of one leg and the partial swelling of the other leg only if it involved both right and left branches of the bifurcation of the vena cava, which would make the thrombosis or pressure area quite low down in the vena cava. The swelling is not suggestive of a thrombotic condition arising from the deep veins in the calf because of the absence of Homans's sign, and we do not have to suppose that it was that when we go on and find a mass, which by the organs it displaces must be a retroperitoneal mass in the location where it could partially obstruct the abdominal vena cava and perhaps also cause thrombosis. If all that is true, the question comes down to the nature of this retroperitoneal mass in a sixty-six-year-old woman, which was not immediately fatal and which caused no severe pain and no fever. The absence of fever and the white-cell count enable us to rule out an inflammatory mass fairly well. If it were an abscess in the retroperitoneal region of sufficient size to displace the organs, as it usually does, it would have to be tuberculosis of the spine, and it is unlikely that the spine would not show some evidence of erosion. So I think we can dismiss that possibility.

If it were a retroperitoneal hemorrhage, we would expect a somewhat lower hemoglobin level and red-cell count and severer pain at the time the hemorrhage occurred. Also, it would have to be a very extensive hemorrhage to form a retroperitoneal hematoma large enough to displace the organs as described. If it were a cyst of that size, it would

almost have to be one of either the kidney or the ovary, and we would expect mention of its being felt on abdominal examination.

That brings us down to neoplasm in the retroperitoneal space as the most likely possibility. Can we go farther and try to guess the nature of the retroperitoneal neoplasm? Sixty-six is definitely in the cancer age, which means less and less as people see malignant tumors in all age groups, but the fact remains that there is a higher incidence in elderly people than in young people. Is there any kind of carcinoma that this could have been? It is very unlikely. There is nothing to make one think of the gastrointestinal tract or the ureter, and I think that we will have to say that it was not a primary cancer in the retroperitoneal space. It was presumably not metastatic cancer in the retroperitoneal space because there were no previous symptoms to suggest the existence of a primary carcinoma, and such a huge metastatic mass would be strange without an obvious explanation for its presence. So it must have been some kind of neoplasm of the sarcoma or lymphoma or lymphosarcoma type, if it was a neoplasm. There is a condition (retroperitoneal lipoma) that I have never seen and that is found in middle-aged people, women more than men, and often contains areas of cancer and sometimes areas of hemorrhage. It becomes very large, and it would be capable of producing this picture, I think. It could be a retroperitoneal sarcoma of almost any type; or it could be a retroperitoneal lymphosarcoma. This patient's age is not against that, and we have no way of knowing which it was but so long as I am quite likely to be wrong anyhow, I think I shall guess that it was a rare disease and say that this woman had a retroperitoneal lipoma with thrombosis of the veins producing edema of the right leg.

Dr. Claude E. Welch: May I ask Dr. Rogers if he would have operated on the patient?

Dr. Rogers: I am ashamed to say that I did not consider that point in studying the protocol. The patient was apparently getting better, and although no diagnosis was possible without operation, I should think it was very questionable how much operation could accomplish in the way of permanent cure. I probably would have to operate to make the diagnosis but would not be hopeful of curing her. Perhaps a course of x-ray treatment would have helped rule lymphosarcoma in or out without operation.

Dr. Robert R. Linton: I should like to say a word about the edema of the right leg. I doubt whether the tumor caused the swelling of the right leg because a tumor mass pressing on the inferior vena cava should cause the left leg to swell also. The unilateral edema suggests to me a deep venous thrombosis of the right leg.

Dr. Wyman: From the x-ray point of view a lipoma might be expected in most cases to show rarefaction. Not necessarily, of course, but that might be a lead against lipoma. This lesion looked homogeneous in density.

Clinical Diagnosis

Retroperitoneal sarcoma.

Dr. Rogers's Diagnoses

Retroperitoneal lipoma.
Venous thrombosis.

Anatomical Diagnosis

Malignant lymphoma, lymphoblastic type.

Pathological Discussion

Dr. Welch: It is an interesting point that Dr. Linton made. We see 3 or 4 patients each year with thrombophlebitis in the extremities as the first sign of abdominal cancer, and we were interested to discover whether or not there was direct involvement of the vena cava in this case to account for the thrombosis. We operated with a diagnosis of retroperitoneal sarcoma. A long transverse incision was made, and we found, as the x-ray film has shown, the kidney displaced downward and laterally. The large tumor was intimately adherent to the vena cava, which was not thrombosed. We suspected the histologic nature of the tumor as we palpated it and proceeded with the excision of the tumor mass. Other small but definitely enlarged lymph nodes were noted about the celiac axis.

Dr. Tracy B. Mallory: The tumor that we received in the laboratory showed a malignant lymphoma of relatively undifferentiated character, which we diagnosed as lymphoblastic lymphoma. Following operation the patient made a smooth convalescence and is now undergoing x-ray therapy.

Dr. Linton: How large was the mass?

Dr. Welch: I should say 11 by 7 by 6 cm.

Dr. Rogers: Do you think that standing on her feet for such a long period was the cause of the episode of edema?

Dr. Welch: We thought that it was.

Dr. Rogers: Was the mass movable with changes of gravity?

Dr. Welch: No; it was firmly fixed.

CASE 34122

Presentation of Case

A sixty-nine-year-old watchman entered the Emergency Ward because of difficulty in voiding of two months' duration.

During this period repeated instrumentation and catheterization were required, and blood clots were passed in the urine from time to time. Voiding was difficult, delayed and in small amounts. Episodes of epigastric pain followed by vomiting were reported, but the history was vague and erratic. Bowel habits were normal and without diarrhea or melena.

A 40-pound weight loss in the six months before entry was reported.

Physical examination revealed an emaciated, pale, drowsy, chronically ill man, with a hot, dry, wrinkled skin. The heart and lungs were not remarkable except for a few extrasystoles. The abdomen was scaphoid and difficult to palpate; some resistance was encountered in the right upper quadrant, but no tenderness, mass or liver edge could be made out. Rectal examination was negative; the prostate was of normal size, with a slightly granular consistence. The left scrotum was enlarged four or five times normal.

The temperature was 101.2°F., the pulse 80, and the respirations 18. The blood pressure was 105 systolic, 60 diastolic.

Examination of the blood revealed a red-cell count of 3,800,000, with a hemoglobin of 8.5 gm., and a white-cell count of 8200. A stool examination showed a ++++ guaiac reaction, and the vomitus a ++ guaiac reaction. Urinalysis disclosed a +++ test for albumin, with numerous red cells and occasional white cells in the sediment. The nonprotein nitrogen of the blood was 45 mg. per 100 cc., the total protein 5.6 gm., the fasting blood sugar 96 mg., the calcium 7.6 mg. and the phosphorus 2.6 mg. per 100 cc. The chloride was 100 milliequiv. per liter, and a van den Bergh reaction was normal. The amylase was 38 units per 100 cc., and the alkaline phosphatase 3.8 units. An intravenous pyelogram showed right-sided calyceal blunting without ureteral dilatation; this was later confirmed by a retrograde pyelogram, with the demonstration of a bladder stone. Chest films and a barium enema were not remarkable. A gastrointestinal series demonstrated an obstruction at the antrum, with an area of marked narrowing 3 cm. in length, but a normal-appearing duodenal bulb was seen. Cystoscopy revealed moderate trabeculation and a 2 cm. oval, granular, whitish stone on the bladder floor; no tumor was seen.

After completion of studies it was agreed that the patient should be prepared for surgical exploration. On the fifth hospital day, however, he developed sudden, severe, nonradiating, right-lower-quadrant and right-upper-abdominal pain, with associated physical findings of lower-abdominal distention, tympany, rumbling peristaltic rushes and marked deep right-lower-quadrant tenderness; there was no spasm or rebound tenderness. Impacted barium was removed from the rectum, with slight relief. An upright abdominal film showed no subdiaphragmatic air and no dilated loops of bowel. A Levine tube was passed, and the patient vomited 1500 cc. of brown watery fluid, which was equivocal on guaiac test. The symptoms subsided gradually, and parenteral fluid therapy was again directed toward surgical preparation. Two days later he had a similar sudden, severe episode, with the same findings and another normal abdominal film. Relief was again obtained by aspiration of gas and 500 cc. of fluid from the stomach.

An operation was performed.

Differential Diagnosis

Dr. Robert R. Linton: As one reads the record, this patient obviously had something much more seriously wrong with him than the genitourinary condition when he came to the Emergency Ward. He had difficulty in voiding of two months' duration. I believe, however, that that had very little to do with the condition for which I am supposed to discuss this case. Obviously, he had a bladder stone, and I assume that that and perhaps some obstruction from the prostate were the reasons for the difficulty in voiding. In addition, he had a mass in the left side of the scrotum due to a large scrotal hernia or hydrocele, probably the latter. These, I think, are unrelated, although it is possible that if it were a hernia, one could connect the episode described later on with an incarceration and perhaps partial obstruction of the small intestine. It is interesting that very little vomiting is mentioned during the hospital admission, and yet the vomitus is reported guaiac positive. It is also significant that the stool examination showed a ++++ guaiac reaction. Those findings suggest that he was suffering from some lesion in the gastrointestinal tract that had produced blood in the stools. The x-ray examination, I think, reveals the source of bleeding, both in the stools and in the vomitus. Before going farther we might see the x-ray films.

Dr. Stanley M. Wyman: The chest appears within normal limits for a patient of this age. The lesion described in the gastrointestinal tract is seen in the region of the antrum and prepyloric region on these two films and is well seen on these two spot films. There seems to be a constant narrowing that does not change in contour. There is a suggestion of a normal mucosal pattern, but that is not definite. The point about the films that interests me is this irregularity in the upper second portion of the duodenum, which is not mentioned in the record. It is a constant finding on all the films, and there seems to be a suggestion of shelf formation distally and possibly proximally on the lesser curvature. On the medial aspect of the duodenum there is an accumulation of barium that may lie in a diverticulum or an ulcer crater. I do not see the duodenal cap adequately outlined on any film. I cannot comment further on that. This brings up the question whether or not there were one or two lesions in the upper gastrointestinal tract. The colon shows nothing remarkable. A film from the pyelogram shows a stone in the bladder. I think the blunting of the calyxes on the right is minimal. The left kidney is displaced downward, but I do not know why.

DR. LINTON: Do you know anything about the six-hour or twenty-four-hour film? Was there any gastric residue?

DR. WYMAN: That is not included in the series of films that I have here.

DR. LINTON: It is certain that one has to take the roentgenologist's opinion of this finding as showing evidence of a lesion in the distal end of the stomach and a questionable lesion apparently in the second portion of the duodenum. Would you say that the duodenal loop is widened at all?

DR. WYMAN: No; there is no widening.

DR. LINTON: I ask that because a wide duodenal loop frequently means a malignant or inflammatory lesion involving the pancreas.

We do not know too much about what happened during the stay in the hospital except that operation was decided on. The patient suddenly developed upper abdominal pain, lower abdominal distention and rumbling peristaltic rushes, and when a Levine tube was passed down the stomach he vomited 1500 cc. of brownish watery fluid. I assume that he must have aspirated some fluid as well as this large amount that he vomited. One-and-a-half liters is considerable residue in anyone's stomach — especially one who is not taking a great deal of nourishment by mouth. The episode apparently repeated itself, and again 500 cc. was aspirated.

It seems to me that the diagnosis in this case is very obvious, and for that reason I am probably wrong. We are dealing with a patient who has a lesion in the pyloric end of the stomach, which constricted the lumen sufficiently to cause dilatation of the stomach with retention of gastric secretions and food taken by mouth. I have ruled out small-bowel obstruction since the small bowel was not dilated. As a matter of fact, when I was a resident here (in the days before the Levine tube was used routinely) I helped one of the visiting men operate on a patient for small-bowel obstruction because of large peristaltic waves seen in the right lower quadrant, and much to our amazement the patient had acute dilatation of the stomach and no small-bowel obstruction whatever. The patient responded very well to simple lavage and drainage of the stomach. It is my opinion that the patient in the case under discussion had a lesion of the distal portion of the stomach involving the pyloric end, which, in view of the positive guaiac test on the stool and vomitus, suggests a malignant lesion. I am unable to rule out or in a lesion involving the second portion of the duodenum, but in view of the fact that we have no evidence in the x-ray report that there is marked constriction in the duodenum, I believe that the lesion is more likely to be in the distal end of the stomach. My diagnosis is carcinoma of the pyloric end of the stomach, with pyloric obstruction.

DR. ALFRED KRANES: If there were a lesion in the second portion of the duodenum, would you consider anything else?

DR. LINTON: One would have to consider carcinoma of the head of the pancreas, which is unusual without some evidence of jaundice due to obstruction of the common bile ducts.

DR. KRANES: I was thinking of lymphoma with multiple lesions, if that observation is correct.

DR. LINTON: That is a good suggestion. I had not thought of a lymphoma here. Malignant lesions of the distal end of the stomach would probably cover it.

DR. WYMAN: I am at a disadvantage because the examination is not complete. Benign ulcer of the duodenum could produce this picture in the duodenum, and there might have been an ulcer of the prepyloric region that had resulted in scarring.

DR. LINTON: The fact that the stool gave a ++++ guaiac reaction is a little against a duodenal ulcer due to cicatricial contraction, because such patients do not bleed much, but again the blood could have arisen from the mucosa of the dilated stomach.

DR. WYMAN: If the duodenal lesion has a crater, with associated spasm, the bleeding is possibly explained.

DR. LINTON: Yes.

CLINICAL DIAGNOSIS

Carcinoma of stomach.

DR. LINTON'S DIAGNOSIS

Carcinoma of pyloric end of stomach.

ANATOMICAL DIAGNOSES

Duodenal ulcer, active.
Chronic gastritis.

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: This patient was explored, and a very large, old, indurated ulcer was found in the second portion of the duodenum on the posterior wall. A subtotal gastric resection was performed, and no lesion was found in the stomach other than a mild hypertrophic gastritis. Following operation attention was finally drawn to the complaint for which he came in. The bladder stone was duly crushed and removed, and a small amount of prostatic tissue around the mouth of the bladder was removed. After multiple operations the patient went home with a good recovery.

DR. KRANES: What was the cause of the right-lower-quadrant pain?

DR. MALLORY: Acute gastric dilatation, so far as we know — nothing else was found.

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COMMUNICATIONS should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston 15, Massachusetts.

DIABETES — A MASS EXPERIMENT IN THE STUDY OF ARTERIOSCLEROSIS

Two papers on diabetes in this issue of the *Journal* bear witness to the continuing importance of the disease despite the advances that have been made in its control. The diabetic group furnishes, in particular, an unusual group for the study of the degenerative diseases, for although its members live on the average for fourteen years after the diagnosis is made, 67 out of 100 succumb to hardening of the arteries. We may expect, therefore, from recent evidence,* that the degenerative changes of old age should be further deferred and life prolonged beyond the present sixty-four years by an organized and intelligent study of this group, employing the most modern methods.

The bounds of the experiment are definite. Here is a homogeneous group of 1,000,000 patients with known and 1,000,000 persons with undiagnosed diabetes, two thirds dying of arteriosclerosis with the average duration of their diabetes now fourteen years, and their average age at death sixty-four years. The extension of any one of these frontiers is an achievement dependent upon the individual efforts of both patient and doctor. Like the athlete and his trainer, success will be found where the partnership between the two has been the closest.

The data already obtained in this mass experiment show its importance. How is it that coronary thrombosis is eight times as frequent in diabetic as in nondiabetic women? Why are calcified pelvic arteries found in 46 per cent of 79 young persons who have had diabetes for twenty or more years with only 1 such case noted in 75 nondiabetic persons of similar age? Of what significance is the demonstration that the chance of obtaining a living child from a pregnant diabetic mother is only 20 per cent if the pelvic arteries are calcified but more than 90 per cent if they are not calcified? Why should 20 cases of calcification of the vas deferens be observed in diabetic patients compared with 1 case in a nondiabetic person?

The participation of endocrinologic factors may be studied since diabetes itself is conditioned by a deficiency of a specific hormone, insulin. Biochemical analyses of humoral factors, of which the lipid cholesterol may be mentioned, are rapidly accumulating. The influence of metabolic and infectious agents is under scrutiny.

The discovery of the cause for the premature advent of degenerative changes of old age in a person with diabetes will have far-reaching consequence for the whole human race.

*Diabetes Exhibit, Interim Session, American Medical Association, January 5–8, 1948.

THE GENERAL PRACTITIONER ORGANIZES

THE general practitioner of medicine, after centuries as the leading exponent of his profession, is at last having efforts made to restore to him some-

thing of this position, even in an age of science that seemed to have passed him by.

The American Medical Association established a section on general practice in 1946, and in June, 1947, on the occasion of the centennial convention of the Association in Atlantic City, the American Academy of General Practice was founded. The wheel has completed its cycle. Each of the major divisions of medicine that split off from the main body of this art has achieved its special rating and its special privileges; the parent and protector of them all has at last been stirred to seek its own salvation.

There have been organizations of general practitioners before now — to wit, every state medical society and the American Medical Association itself, a hundred years ago. This is the first time, however, that general practice has raised its voice to be heard throughout the nation, as distinct from the voices of its offspring — perhaps in self-protection against those lesser, if more sparkling, satellites.

The purposes of the Academy as avowed in its constitution are praiseworthy: to promote and maintain high standards of the general practice of medicine and surgery; to encourage and assist young men and women in preparing, qualifying and establishing themselves in general practice; to preserve the right of the general practitioner to engage in medical and surgical procedure for which he is qualified by training and experience; to assist in providing postgraduate study courses for general practitioners; and to encourage and assist practicing physicians in participating in such training.

To be eligible for membership a physician must be engaged in general practice; he must be licensed in the state in which he practices; he must be of the usual high moral and professional character. He must have had at least one year of rotating internship at an approved hospital or the equivalent in postgraduate training, and he must have been in general practice for at least three years.

This new organization of general practitioners is not novel, nor are its purposes in any way original, unless we consider it as being quite different in its aim and ideals from the sometime association of physicians who called themselves Asklepiads. Threatened groups or groups that wish to extend their influence have always organized, and organization is as old as the family, the tribe or the pack.

The general practitioner, hardy and independent as he is, has had his livelihood threatened by better organized minorities. He has been passed by, overridden and denied the privileges of those certified by "boards" and has found access to hospitals difficult. Organization for self-protection and *self-improvement* has been necessary. In this organization, however, he does not wish to be patronized, and he does not need to be flattered. He knows his worth to the community, and if the community does not know it, it can be taught.

NEGRO HEALTH WEEK

National Negro Health Week has been planned for April 4 to 11 by the Office of Negro Health Work of the United States Public Health Service. This particular observance is not the result of any recently exploited circumstances; the movement was originated in 1915 by the Negro race's own great leader, Booker T. Washington, whose birthday on April 5 will fall within the designated period.

After Dr. Washington's death the program that he initiated was annually conducted at Tuskegee Institute, at which time Founder's Day was celebrated and the National Medical Association and the John A. Andrew Clinical Society held their meetings. At this time, also, clinics were held at the Institute's John A. Andrew Memorial Hospital, the gift of members of the family of Massachusetts's great abolitionist and Civil War governor. A number of Northern physicians have been guests at these gatherings and have carried away pleasant recollections of the hospitality and courtesy extended to them.

The current health week, while bringing to light some of the problems that confront the Negro, will also, it may be hoped, discover more and more helping hands extended toward him — a greater spirit of co-operation in furthering his adjustment to an environment not originally of his own choosing.

The President's Committee on Civil Rights has recently issued its report proposing "the enactment by the States of fair health statutes forbidding discrimination and segregation based on race, creed,

color or national origin, in the operation of public health facilities."

This is all very well, and fair laws make fine reading. What is needed, however, is not so much new laws as a new spirit of tolerance and co-operation and understanding. Through all the history of the world there can be found running an unbroken thread of man's humanity to man. When that thread can be broadened into a convincing pattern then may countless thousands cease to mourn.

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

FLEMING — Edwin R. Fleming, M.D., of Medford, died on March 4. He was in his sixty-ninth year.

Dr. Fleming received his degree from Jefferson Medical College of Philadelphia in 1904. He was a member of the New England Obstetrical and Gynecological Society and a fellow of the American Medical Association.

His widow survives.

HEALY — Thomas R. Healy, M.D., of Newburyport, died on February 25. He was in his seventieth year.

Dr. Healy received his degree from Dartmouth Medical School in 1899. During World War I he was chief of the X-Ray Department of the United States Marine Corps and the United States Navy. He was a member of the American Roentgen Ray Society, New England Roentgen Ray Society, Radiological Society of North America and American College of Radiology and was a fellow of the American Medical Association.

A brother, a nephew and a niece survive.

HOWE — Oliver H. Howe, M.D., of Cohasset, died on March 1. He was in his eighty-eighth year.

Dr. Howe received his degree from Harvard Medical School in 1886. He was a former president of Norfolk South District Medical Society.

Four sons survive.

RICE — John Dexter Rice, M.D., of West Boylston, died on October 4. He was in his thirty-third year.

Dr. Rice received his degree from Tufts College Medical School in 1940.

His mother, father, three brothers, a son and two daughters survive.

A HUNDRED YEARS AGO

The following remarks, by Dr. H. J. Bigelow, of Boston, on a subject first brought to the notice of the profession by himself, in the pages of this *Journal*, are entitled to consideration. He believes that profound narcotism can always be produced by the use of ether or chloroform and that within a short time, no surgeon will commence a formidable or nice operation upon a patient who has not arrived at this stage of *anaesthesia*. When ether is used, inhalation should be of *air impregnated with ether, and passing through it, and not of ether alone*, as from a sheet, bag or sac. He has had a good opportunity of testing the effects of chloroform in his own and other operations, and, indeed, has used no ether since its introduction. It seems to him to be thus far identical with ether in its effects, much stronger and portable, it does not infect the clothes, is less irritating to the lungs, and is at first quite palatable to the patient. In his opinion, it must supersede "ether" of which it is but a variety. — One achievement prepares the way for another and we are again taken by surprise with a new preparation which is to be known under the name of *Collodion* — being a solution of *gun* cotton in ether. Mr. Samuel L. Bigelow, a senior student at the Harvard Medical School informs us that from Dr. Charles T. Jackson he learned the manner of preparing it, for Dr. Jackson had remarked upon it and exhibited specimens before the National History Society, in Dec. 1846 or Jan. 1847, and enumerated various uses to which it might be applied — among others, as a brilliant varnish. For this use Mr. Bigelow soon after prepared a bottle, according to the directions. While engaged in employing it in this way, he accidentally smeared with it a fresh wound on his finger. The smarting called his attention to it, and he endeavored immediately to rub it off. It had dried, however, instantaneously, and remained on. The smarting very soon ceased, and when the film was removed, perfect union had taken place. Since this time, the efficacy of this preparation as a dressing for wounds has been tested, especially those which it is desirable to unite rapidly, by first intention. *Collodion* would seem to possess very eminently, all the requirements for producing such a union. Mr. Bigelow is informed that a series of experiments are being now made at the Mass. General Hospital, by the surgeons in attendance, who will be soon able to test its value and range of application. — Speaking of the Hospital, a copy of the late report of the institution was sent to the editor several days since. From page 10 to 46, the trustees have devoted to the history of the discovery of ether inhalation; and they have taken strong ground, too, in their 4th conclusion, in saying, "The whole agency of Dr. Jackson in this matter appears to consist in his having made certain suggestions, which led Dr. Morton to make the discovery — a discovery which had for some time been the object of his labors and researches." Although drawn up with an air of candor and fairness, this report will be memorable in the series of annual accounts of that beautiful establishment from the circumstance that it bears a history of the ether war. There are no more indications of peace between the rival candidates for favor, than there is between this Government and Mexico. — Another donation of $100,000 has nearly found its way into the treasury of the institution. At this rate, it will ultimately become immensely rich. Five hundred medical students should be daily learning the details of their profession there. — We take this opportunity to men-

tion, that when a communication is intended for a leading article in this *Journal*, it should be received at the Editor's office not later than Monday of the week preceding that in which the article is to be published. Two pages of each number are left open till Monday morning, which is the latest period for the receipt of brief notices, etc. — Extracted from the *Boston Medical and Surgical Journal*, March, 1848.

R. F.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

DEPARTMENTAL PUBLICATIONS

The following is a list of publications sent out regularly by the Massachusetts Department of Public Health. They are available to anyone upon request.

Blood Donor News (bimonthly) contains news regarding schedules of the mobile unit, collection and distribution of blood, and progress and changes in the program.

Cancer Bulletin, a quarterly bulletin for physicians, contains abstracts of important papers on cancer research, diagnosis and treatment.

Cancer Tidings, issued bimonthly, is a news letter sent out to members of the co-operative cancer-control committees giving the latest news on cancer-control programs being carried on in the Commonwealth.

Communicable Disease Information, sent out weekly, gives up-to-the-minute news of the reported cases of communicable diseases in Massachusetts.

Contact, a quarterly bulletin prepared by the Division of Maternal and Child Health containing articles and recommendations on school health work, is primarily directed to school superintendents and school nurses.

News Letter, a monthly bulletin, contains articles and news of general interest to all health workers.

V. D. Bulletin, a quarterly for physicians, is designed to disseminate information regarding current advances in the treatment and control of venereal diseases.

APPOINTMENT OF DR. FIUMARA

Dr. Nicholas J. Fiumara has been appointed director of the Division of Venereal Diseases of the Massachusetts Department of Public Health, after certification by the Division of Civil Service of the Commonwealth. Dr. Fiumara is a graduate of Boston College and Boston University School of Medicine. Since his return from service with the Navy, Dr. Fiumara has received the degree of master of public health from the Harvard School of Public Health. He is a fellow of the Massachusetts Medical Society and the American Medical Association and a member of the Massachusetts Public Health Association and the American Public Health Association.

MISCELLANY

NATIONAL HEALTH ASSEMBLY

A National Health Assembly will be held in Washington from May 1 to 4, according to Oscar R. Ewing, federal security administrator. The Assembly is the result of President Truman's message of January 30, requesting the development of national health goals for the next ten years.

The activities of the Assembly in initiating this ambitious program will be largely in the form of panel discussions, each panel to explore fully a specific phase of the health problem. An anticipated contribution of the Assembly will be a clearer picture of how much agreement there is in certain supposedly controversial health fields.

BELGIUM HONORS DR. RICHARD P. STRONG

The Belgian ambassador, Baron Robert Silvercruys, in an intimate ceremony at Dr. Richard P. Strong's residence on February 7, presented him with the cross of Officer of the Royal Order of the Lion. This award, which had been granted by an executive order of February 24, 1947, was in recognition of the pioneer work that Dr. Strong had performed in 1926 and the following year, when he led a medico-biologic expedition into Liberia and the Belgian Congo.

The Order of the Lion is one of the highest ranking Belgian decorations. It was conferred on Dr. Strong through the offices of the Secretary for Colonies and indicates the high esteem in which he is held in Belgian scientific and colonial circles.

MARKLE FOUNDATION AWARDS

Among the sixteen scientists appointed as the first group of scholars in Medical Science under the John and Mary R. Markle Foundation plan are Christian B. Anfinsen, Ph.D. (A.B., Swarthmore College; S.M., University of Pennsylvania; Ph.D., Harvard Medical School), to Harvard Medical School in the field of biochemistry; Edward J. Beattie, Jr., M.D. (A.B., Princeton University; M.D., Harvard Medical School), to George Washington University School of Medicine in the fields of surgery and cardiorespiratory physiology; and Henry D. Hoberman, M.D. (A.B. and Ph.D., Columbia University; M.D., Harvard Medical School), to Yale University School of Medicine in the field of biochemistry, particularly in the study of compounds by the use of isotope tracers.

APPOINTMENT AT COLUMBIA UNIVERSITY COLLEGE OF PHYSICIANS AND SURGEONS

Dr. Otto Lowenstein was recently appointed clinical professor of neurology at Columbia University College of Physicians and Surgeons.

CORRESPONDENCE

BILIRUBIN AND THE RENAL FILTER

To the Editor: I have read with great interest Dr. Lawrence E. Young's review "Current Concepts of Jaundice, with Particular Reference to Hepatitis," which appeared in the August 14 and 21 issues of the *Journal*. On a single point, however, a fundamental misunderstanding of the facts is put forward in this valuable study.

Dr. Young is of the opinion that the occurrence of bilirubinuria in the different forms of jaundice is explained by the fact that bilirubin globin — the "indirect" bilirubin of

hemolytic jaundice and retention jaundice — cannot pass the renal filter, whereas the free sodium bilirubinate ("direct" bilirubin) present in the serum of patients with regurgitation jaundice does. This opinion is quite erroneous, for it has long been known that all bilirubin present in serum is bound to the albumin fraction of the serum protein — be it globin or common serum albumin — and consequently does not filtrate or pass by diffusion the kidney membrane or any other semipermeable membrane. This has been shown by dialysis, electrophoresis and ultrafiltration, as pointed out by Snapper and Bendien in their articles entitled "Abtrennung von Serumkolloiden durch Ultrafiltration" (*Acta brev. Neerlandica* **1**:69-71, 1931) and "On physico-chemical condition of bilirubin in bloodserum and urine" (*Acta med. Scandinav.* **98**:77-82, 1939), by Bennhold in his paper entitled "Über die Vehikelfunktion der Serumeiweisskörper" (*Ergebnisse d. inn. Med.* **42**:273-375, 1932) and by Pedersen and Waldenström in a study entitled "Studien über das Bilirubin in Blut und Galle mit Hilfe von Elektrophorese und Ultracentrifugierung" (*Ztschr. f. physiol. Chem.* **245**:152-162, 1937). The results of these investigations are in perfect agreement with the well known facts that cerebrospinal fluid, sweat, saliva, tears and almost all secretions and excretions, with the exception of urine and bile, are free from bilirubin even in long-standing severe jaundice, as demonstrated in the literature cited in my paper "Bilirubin in urine and other secretions apart from the bile and in the cerebrospinal and eye liquors" (*Acta physiol. Scandinav.* **10**:355-365, 1945). Bilirubin is thus a rather singular substance from the point of view of the kidney physiologist, since it is not excreted by filtration in the glomeruli but solely by secretion in the renal tubuli. The linkage between bilirubin and the serum albumins is very firm and can only be loosened by means of the active cellular work of the liver cells and the cells of the tubuli of the kidneys. This linkage of the serum bilirubin to the serum albumins — including possibly globin from hemoglobin — is also of great interest for the understanding of the pathogenesis of jaundice. For it is very difficult to understand how bilirubin passes through the capillaries into the tissue spaces and colors the various yellow tissues. I have tried to solve this difficult question by means of a provisional hypothesis in my recent paper "Pathogenesis and different forms of jaundice" (*Acta med. Scandinav.* **128**:25-41, 1947).

TORBEN K. WITH, M.D.

Rigshospitalet
Copenhagen

Dr. With's letter was referred to Dr. Lawrence E. Young, whose reply is as follows:

To the Editor: Although it is now recognized that some substances are excreted by the kidney only as a result of work by the tubular cells, the term "renal filter" is still rather liberally applied in references to the kidney in current medical literature. Boyd, for example, in discussing "indirect" bilirubin in his *Textbook of Pathology* (fourth edition, P. 542) states: "This type of bilirubin cannot pass the kidney filter." On Page 541 of the same text the following statement is found: "If the altered bilirubin is then reabsorbed into the blood, as in obstructive jaundice, it is able to pass the barrier of the renal filter and appears in the urine." Numerous references of this sort could be cited, and in addition the term "renal barrier," which has similar connotations, is currently employed by many writers. Hanger, for instance, states in Cecil's *Textbook of Medicine* (seventh edition, P. 856) that "the delayed indirect fraction is retained by the renal barrier."

I agree with Dr. With that, in the light of present knowledge, more specific terms might well be used in describing various types of renal activity. It should be made clear, however, that in my review on jaundice I was merely following current usage of the term "renal filter" and was not expressing a personal opinion that bilirubin is excreted by glomerular filtration.

Dr. With's informative and thought-provoking paper, "Pathogenesis and Different Forms of Jaundice," raises a number of questions that can be answered only by further experimental and clinical observations. In particular, the manner and extent of the binding of bilirubin by protein and the mechanism by which bilirubin leaves the circulation are not yet clear. The active separation and excretion of protein-bound bilirubin by renal tubular cells, if it occurs, is without precedent according to modern concepts of renal physiology.

Anyone interested in jaundice will profit from consideration of the material presented in Dr. With's recent review.

LAWRENCE E. YOUNG, M.D.

Strong Memorial Hospital
Rochester, New York

RESTORATION OF LICENSE

To the Editor: At a meeting of the Board of Registration in Medicine held February 19, it was voted to restore the registration to practice medicine to Dr. Nathan Gaber, 129 Mt. Vernon Street, Boston, as of February 21, 1948.

H. QUIMBY GALLUPE, M.D., *Secretary*

State House
Boston

"NEGATIVE BRONCHOSCOPY"

To the Editor: As an ardent follower for over ten years of the Case Records of the Massachusetts General Hospital, I cannot help taking this occasion to raise a question concerning certain statements appearing under Case 34022 in the issue of January 8. This was a case of bronchogenic carcinoma occurring in a lower-lobe bronchus. There was peripheral suppuration and contraction of one of the basal segments, a situation commonly referred to loosely as "atelectasis." There was nothing particularly remarkable about the case as a whole. Bronchoscopy had revealed an inflamed, edematous mucosa with marked obstruction and some purulent secretion. The lobectomy specimen revealed carcinoma and rather extensive bronchiectasis. The surprising thing was the comment by Dr. Donald King, seconded by Dr. Benedict, that he could not recall such a case with "a negative bronchoscopy." I think anyone who has done much chest work will agree that such a situation is not only not rare but also relatively common among a large group of bronchogenic carcinomas, and that many of them cannot be positively diagnosed by the most expert bronchoscopists prior to exploratory thoracotomy. Furthermore, the bronchoscopy was not actually "negative," except in the sense that it did not clearly reveal tumor. It seems probable that the statement conveyed a different impression than was actually intended. In any event it was most certainly inaccurate.

F. J. LOVELOCK, M.D.

Chest Service
Bellevue Hospital, New York City

Dr. Lovelock's letter was referred to Dr. Donald S. King, whose reply is as follows:

To the Editor: Thank you for referring Dr. Lovelock's letter to me. He has just cause for alarm. The statement as published: "I cannot remember any case with cancer in a bronchus with a negative bronchoscopy . . . " is of course not true. I cannot be sure what I said. What I meant to say was: "I cannot remember any case with cancer in one of the segmental bronchi to the *basal* segment of a *lower* lobe in which we were unable to make a correct diagnosis by means of bronchoscopy." I have not been able recently to review our series of some hundreds of cases of primary bronchogenic carcinoma, but so far as my memory goes the statement as corrected above must still stand. These segmental bronchi are usually easily visualized at bronchoscopic examination. I did not make it clear that I was distinguishing between cancer in the basal segment in the lower lobe and that occurring in the dorsal segment of the lower lobe, the middle lobe or the upper lobe. Bronchoscopic visualization is much more difficult in these areas.

DONALD S. KING, M.D.

1101 Beacon Street
Brookline, Massachusetts

HEALTH MENACE IN CROWDED TRANSPORTATION FACILITIES

To the Editor: It is to be hoped that the members of the Massachusetts Legislature will realize that the problem of meeting the transportation needs of southeastern Massachusetts as a result of the announced discontinuance of train service on the Old Colony Railroad has its medical as well

as its economic aspects. If the Metropolitan Transit Authority takes over this responsibility and continues its policy of furnishing 60 or even as many as 80 seats for every 100 passengers, it will mean crowded cars and many passengers standing. Crowded cars afford an opportunity for the easy and rapid spread of respiratory infections during a period when an epidemic is prevailing. The tired worker or businessman, who must stand all or much of his way home, is quite susceptible to infection; his disposition is not improved by a trying trip from work, and he does not contribute to a happy home. It makes one shudder to think that many more thousands may be added to the crush and pushing in already overcrowded trains and subway stations.

Sound public-health policy demands a seat for every commuter. It demands protection of the older and handicapped person in the rush for the car door and seats. It is evident that adequate and comfortable transportation facilities will reap a benefit in the health and efficiency of the public that will compensate for possible deficits in operation of transportation facilities.

HAROLD L. HIGGINS, M.D.

322 Franklin Street
Newton

BOOK REVIEWS

Devil by the Tail. By Langston Moffett. 8°, cloth, 431 pp. Philadelphia: J. B. Lippincott Company, 1947. $3.00.

This novel tells the story of a man afflicted with a perpetual desire for alcohol. He traveled the world over and finally after fifteen years of drunkenness conquered his desire by self-renunciation and with the help of love. This powerful story is well written, and the plot well sustained to the end. It should be in all special collections on alcohol.

Medicine in the Changing Order. Report of the New York Academy of Medicine Committee on Medicine and the Changing Order. 8°, cloth, 240 pp. New York: The Commonwealth Fund, 1947. $2.00.

The Committee on Medicine and the Changing Order was organized in 1943 with a membership of thirty-three physicians and seventeen representatives of allied professions and lay persons. The physicians were chosen because of their interest in medical education and public health. The lay members were selected from the fields of ministry, law, social welfare, hospitals, insurance, labor and industry. The objectives of the research were defined as follows, "To be informed on the nature, quality, and direction of the economic and social changes that are taking place now and that are clearly forecast for the immediate future; to define in particular how these changes are likely to affect medicine in its various aspects; to determine how the best elements in the science of medicine and in its services to the public may be preserved and embodied in whatever new social order may ultimately develop." After a preliminary study and investigation lasting sixteen months, eleven subcommittees were formed to study especially medical education and graduate and postgraduate medical education; internship; the hospital; administration of public-health services; extension of medical services; the cost of diagnostic and consultant services; industrial medicine; rural medicine; nursing; and dentistry. The committee also selected the titles and authors of twelve monographs to be published by the Commonwealth Fund. These monographs have been noted or reviewed from time to time in these columns.

This general report summarizes the work of the committee in the various fields mentioned above. The report opens with a chapter on the origins of present problems in American medicine and concludes with one on "the method and goal." The committee does not approve compulsory health insurance at present and disapproves any form of prepaid, full-coverage insurance to be applied as suitable for all sections of the country.

In an over-all program the following principles are emphasized: in extending medical service and perfecting its organization, quality must be preserved; provision of public-health services is a primary essential; improvement in medical service requires effective use of hospitals with adequate facilities; success will require trained professional and nonprofessional personnel; for optimal results, organization and co-operation of physicians are required; in the improvement of medical services, voluntary prepayment plans are needed; the goal should be comprehensive medical service; extensive education for both physicians and the public will be required; progress in the extension of medical service must be varied and adapted to the needs of the community; and finally Government aid will be required. Each of these points is discussed at length. The report and collateral volumes are well published in a uniform series. The New York Academy of Medicine and the Commonwealth Fund are commended for completion of this valuable study and its publication in an inexpensive form, no volume costing more than $2.50, the average price being $1.61 a volume and the price of the complete set being $20.25. The series is highly recommended for all libraries, medical and general.

Rhinoplasty and Restoration of Facial Contour: With special reference to trauma. By Jacques W. Maliniac, M.D. 8°, cloth, 327 pp., with 214 illustrations. Philadelphia: F. A. Davis Company, 1947. $7.50.

As the title of this book indicates, the author has made an attempt to cover the entire field of traumatic surgery of the nose, from the repair of simple septal deviations to the complex reconstruction of nasal losses.

The book, essentially a monograph describing the author's approach to the various types of nasal deformities of traumatic origin, is divided into thirteen chapters covering 312 pages. The general arrangement of the chapters is good. The volume is well illustrated with photographs and explanatory diagrams. The classification of deformities is somewhat confusing. The diagrams and their legends are not always clear but on the whole are good.

The author justly condemns the use of complicated appliances in the correction of nasal deformities and fractures. However, the reviewer find that the author contradicts this point when he describes a rather complicated and wholly unnecessary method for the immobilization of comminuted nasal fractures on Pages 94 to 97.

Chapters VI and VII are particularly good. In the former the various types of skin grafts, flaps and supporting structures used in rhinoplasty reconstruction and the relative merits of each are described; the discussion of the place for transplantation of cartilage and bone, as well as the sequelae when used improperly, is well taken. The latter chapter, which describes the severe types of septal malformations and their correction, should prove useful to many rhinologists.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Laboratory Manual of Microbiology for Nurses. By Elizabeth S. Gill, S.B., instructor in nursing, Department of Nursing, College of Physicians and Surgeons, Columbia University; and James T. Culbertson, Ph.D., professor of bacteriology and parasitology, University of Arkansas School of Medicine. 4°, paper, 116 pp., illustrated. New York: G. P. Putnam's Sons, 1947. $1.50.

The authors of this manual believe that nurses should be taught the proper methods of handling pathogenic bacteria, and the working exercises in the manual are designed to serve as guides in such instruction under proper supervision. Beginning with work on nonpathogenic micro-organisms for the purpose of teaching the student proper technics and procedures, and the use and care of the microscope, the student is carried forward to the study of the important families of bacteria, the spirochetes, yeasts and molds, protozoans, helminths and arthropods. Two appendixes list reagents and solutions, and sources of supply for materials. A list of books for reference concludes the volume. The material is well and conveniently arranged, and the manual should prove valuable for its indicated purpose.

Preoperative and Postoperative Care. By William J. Tourish, M.D., demonstrator of surgery and chief clinical assistant in surgery, Jefferson Medical College and Hospital; and Frederick B. Wagner, Jr., M.D., instructor in surgery and assistant in surgery, Jefferson Medical College and Hospital. With a foreword by Thomas A. Shallow, M.D. 8°, cloth, 338 pp., with 87 illustrations. Philadelphia: F. A. Davis Company, 1947. $6.00.

This manual was written to help the intern in his routine work. The procedures recommended are those followed generally in large hospitals throughout the country. In addition to sections on general preoperative and postoperative care and for specific regions, there are chapters on the urologic, neurosurgical and gynecologic patient. The standard dosages of drugs are quoted for the average patient. The material is well organized, and the typography is excellent. The heavy coated paper is not suitable for this type of book. The work should prove valuable for those for whom it was written.

A Penicilina por via arterial nas osteomielities. By Eurico B. Ribeiro, Diretor do Sanatório São Lucas. 12°, paper, 124 pp., with 25 illustrations. São Paulo: São Paulo Editora S. A., 1947.

This excellent monograph written in Portuguese, on the treatment of osteomyelitis by the arterial injection of penicillin is worthy of translation into English for the benefit of English-speaking physicians. The early chapters review the literature on an international basis and discuss the method and advantages of arterial injection of penicillin. A chapter on clinical observations reviews 6 cases in detail and is illustrated with a number of radiographs. The final chapter is a summary, and the author concludes that the procedure is of value in both acute and chronic osteomyelitis and that the arterial-injection method is to be preferred to other methods of administration. A bibliography concludes the pamphlet. An index, especially to this foreign-language publication, would have been valuable. The printing is well done with a good-sized type on good paper. The work should be read by all surgeons interested in the subject.

Transactions of the American Society for the Study of Sterility, 1946. 8°, paper, 174 pp. Portland, Oregon: The Western Journal of Surgery Publishing Company, 1947.

The first volume of transactions of the new society on sterility presents seventeen papers on varying aspects of the subject. All the papers, except one, deal with the subject in human beings. The papers are short and concise. The volume is well published and should be in all medical libraries.

Una Epidemia de Peste Bubónica en el Siglo XVI. By Dr. José Vines Ibarrola. 8°, paper, 133 pp. Pamplona: Editorial Aramburu, 1947.

Dr. Ibarrola in this monograph has made a comprehensive study, based on original documents, of the outbreak of bubonic plague occurring in Pamplona in 1599. He has compared this epidemic with those occurring in Fuenterrabia in 1597, in Santander in 1597 and in Milan in 1630; he discusses the medical aspects, epidemiology, sociology and prophylaxis, including the legal and religious factors. This small monograph should be included in all medical-history collections.

Introduction to Medical Psychology. By L. Erwin Wexberg, M.D., director, Bureau of Mental Hygiene, District of Columbia. 12°, cloth, 171 pp. New York: Grune & Stratton, 1947. $3.50.

This short text was primarily written for medical students to supplement their course on the subject in the medical-school curriculum. It should also prove of value to physicians who wish to learn something of psychology in relation to medicine. The subject matter is based on a course of lectures given by the author to undergraduate medical students over a period of eight years. The material is well organized, and appended to each chapter is a list of references for further reading. Indexes of authors and subjects conclude the volume. It is well printed with a good type, on good light paper.

Études sur Arnaud de Villeneuve. Vécu de 1240–1311. By René Verrier, membre associé de l'Institut International de Sociologie. 4°, paper, 86 pp., with 6 plates. Leiden: E. J. Brill, 1947.

In this monograph Verrier has made a study of the documents relating to the family of Arnoldus de Villa Nova with the hope of determining where he was born — in Catalan or in France. Arnoldus was an important physician of the thirteenth century and a writer of note. Likewise, studies are made of his nephews, Jean Blaise and Armengaud Blaise. The first, a surgeon and a capitalist, wrote five works on medicine and surgery. Armengaud became a physician and writer of distinction. He was responsible for ten different works, translations of such classical authors as Avicenna, Averroes, Galen and Maimonides. Verrier draws an interesting comparison between his work as a translator and that of Moses Ibn Tibbon, the famous translator of Maimonides. This important historical monograph should be in all history collections, medical and general.

Ocular Therapeutics. By William J. Harrison, Pharm.D., M.D., associate professor in ophthalmology, Jefferson Medical College, chief, Ophthalmological Clinic, Jefferson Hospital, and attending surgeon, Wills Hospital, Philadelphia. 8°, cloth, 112 pp. Springfield, Illinois: Charles C Thomas, 1947. $3.50.

This pocket manual is devoted to drugs and prescriptions used in ophthalmic practice. It is designed as a ready reference source in the writing of prescriptions and should prove useful to the young physician beginning practice. The material is well arranged and up-to-date, including vitamins, sulfonamides and penicillin. The volume is well published in every way.

Kompendium der parasitischen Würmer in Menschen. By Hans A. Kreis, Privatdozent der Parasitologie an der Universität Bern. 8°, cloth, 136 pp., with 70 illustrations. Basel: Benno Schwabe und Co., 1947. Swiss frcs. 10.

Dr. Kreis in this compendium divides his text into four parts: general; diagnosis of helminthiasis; special, dealing with the trematodes A, cestodes and nematodes; and a zoologic list of the worms noted in the text. In the general part of the text, the author discusses parasitism, the biology of human parasites, the general symptoms and therapy and prophylaxis in general. Under diagnosis he deals with diagnostic methods applied to the feces, urine, sputum, blood and tissues, as well as serologic diagnosis. In the special part each parasite is discussed individually. The text is condensed and well written in easy German. The publication is excellent and approximates prewar standards. The manual is recommended for all medical libraries.

And Never Goodbye. By Robert J. Kuhn. 8°, cloth, 276 pp. New York: D. Appleton–Century Company, Incorporated, 1947. $2.75.

This novel tells the story of the courtship, honeymoon and married life of a psychopathic woman and a man afflicted with a cardiac condition. The tale is told in an introspective manner covering five years, but the action takes place in the short period prior to the admission of the woman to a hospital for the mentally disordered. The book is well written and should be in medicoliterary collections.

New Fields of Psychiatry. By David M. Levy, M.D., assistant professor of psychiatry, College of Physicians and Surgeons, Columbia University. 8°, cloth, 171 pp. New York: W. W. Norton and Company, Incorporated, 1947. $2.75.

Dr. Levy discusses the new trends in psychiatry beginning with the child-guidance movement in 1920 and ending with the present-day utilization of political psychiatry by the United States Military Government in Germany. In addition to these topics, the text deals with comparative, educational, industrial and military psychiatry; delinquency and criminology; social work; and personnel selection. A list of references and an index end the volume. As a survey of modern tendencies in psychiatry the book should prove useful to medical libraries.

NOTICES

ANNOUNCEMENTS

Dr. Fairy P. Brown announces the removal of her office to 289 State Street, Springfield.

Dr. Harold M. Constantian announces the removal of his office to 507 Main Street, Worcester.

Dr. P. N. Papas announces the removal of his office to 199 St. Paul Street, Brookline.

EDWARD K. DUNHAM LECTURES

The Faculty of Medicine of Harvard University has announced that the following lectures on the general topic "Aspects of Microbial Physiology" will be delivered by Dr. André Lwoff, head of the Department of Microbial Physiology, Institut Pasteur, Paris, under the Edward K. Dunham Lectureship for the Promotion of the Medical Sciences:

Monday, March 22. C_4 Dicarboxylic Acids in Bacterial Metabolism.

Wednesday, March 24. Visible Self-Reproducing Cytoplasmic Units in the Life Cycle of Parasitic Ciliates.

Friday, March 26. Aspects of Biochemical Evolution.

These lectures will be held in the amphitheater of Building E, Harvard Medical School, at 5 p.m. on the days indicated.

NEW ENGLAND HEART ASSOCIATION

The next meeting of the New England Heart Association will be held at the Beth Israel Hospital on Monday, March 29, at 8:15 p.m. Dr. Herrman L. Blumgart will preside.

PROGRAM

The Occurrence and Significance of Dilatation of the Aorta Distal to the Area of Coarctation. Dr. Felix Fleischner.

Left Bundle-Branch Block Without Clinical Evidence of Organic Heart Disease. Drs. Mark D. Altschule and A. Stone Freedberg.

Studies of Coronary-Artery Perfusion in Normal and Diseased Hearts. Drs. Paul N. Zoll and David Dresdale.

Observations on the Carotid Sinus and Angina Pectoris. Drs. A. Stone Freedberg and Joseph E. F. Riseman.

The Significance of the Prothrombin Time in the Evaluation of Dicumarol Therapy. Drs. Benjamin Alexander, André de Vries and Robert Goldstein.

Observations on the Syndrome of Short PR Interval with Abnormal QRS Complexes and Paroxysmal Tachycardia. Drs. Louis Wolff and Paul D. White.

Interested physicians and medical students are cordially invited to attend.

AMERICAN ASSOCIATION OF INDUSTRIAL PHYSICIANS AND SURGEONS

The annual meeting of the American Association of Industrial Physicians and Surgeons will be held in Boston from March 30 to April 1, inclusive. The program, which was developed by members of the Council of Industrial Health, Massachusetts Medical Society, is as follows: on Tuesday, March 30, medical and surgical clinics will be conducted at the Massachusetts General Hospital from 9:30 a.m. to 12 m. and at the Boston City Hospital from 2 to 4 p.m.; and in the morning, afternoon and evening of Wednesday, March 31, and Thursday, April 1, three will be devoted to meetings at the Hotel Statler, with selected papers and discussions on common and unusual problems confronting the physician engaged in industrial medicine, with particular emphasis on the rehabilitation of the injured worker.

Further information regarding the program may be obtained from Dr. D. G. Lynch, 245 State Street, Boston, Massachusetts.

INTERNATIONAL SOCIETY OF HEMATOLOGY

The biannual meeting of the International Society of Hematology will be held at the Hotel Statler, Buffalo, New York, from August 23 to 26.

The following time has been tentatively allotted for symposiums and presentations: half a day on general subjects, including radioactive and stable isotopes in hematology; half a day for problems and diseases related to red cells; half a day for problems and diseases related to white cells; one day for immunohematology, Rh-Hr (CDE-cde) antigen and antibodies and hemolytic anemias; half a day for coagulation problems and hemorrhagic diseases; and half a day for a business meeting. Scientific exhibits will be presented in the south wing of the seventeenth floor of the Hotel Statler.

All scientific sessions and exhibits will be open to scientists interested in hematology, including members of the medical profession and branches of science dealing with hematology, such as biochemistry, biophysics, genetics and immunology.

Communications and applications concerning membership will be received by the following members of the membership committee: Dr. William Dameshek, Chairman, 25 Bennet Street, Boston, Massachusetts, for the United States; Dr. M. Bessis, Laboratoire de Recherches, Du Centre National de Transfusion Sanguine, 53, Boulevard Diderot, Paris, France; Dr. Robert R. Race, Lister Institute, Chelsea Bridge Road, London SW. 1, England; Dr. Ludwik Hirszfeld, Institute of Medical and Microbiological Science, Wraclaw, Poland; Dr. Ignacio Gonzales Guzman, University of Mexico, College of Medicine, Mexico, D. F., Mexico; Dr. Walter Cruz, Instituto Oswaldo Cruz, Caiza Postal 926, Rio de Janeiro, Brazil; Dr. Alfred Pavlovsky, Ancherena 1710, Buenos Aires, Argentina; Dr. Theodore Waugh, McGill University, Montreal, Quebec; Dr. Berger Broman, Royal Caroline Medical School, Stockholm, Sweden; Dr. C. R. Das Gupta, Hematology Department, Calcutta School of Tropical Medicine, Calcutta, India; Dr. Luis Sandoval S., Instituto de Histologia de la Universidad de Concepsion, Santiago, Chile; Dr. Rod Sirivejkul, Army Medical Department, Bangkok, Siam; Dr. Carl Rohr, Medizinischen Universitatsklinik, Zurich, Switzerland; Dr. Moises Chediak, Laboratorio Chediak, 23 No. 654 Esq. A., Banos Vedado, Havana, Cuba; Dr. G. di Guglielmo, Director of Medical Clinics, University of Naples, Policlinico, Napoles. Italy; and Dr. Henrik Dam, Danmarks Tekniske Hojskole, Biologisk Afdeling, Ostervolgade 10'' Trappe L, Kopenhagen, Denmark.

Those interested in attending the meetings may communicate with Dr. Sol Haberman, secretary, The William Buchannan Blood Center, Baylor Hospital, Dallas, Texas.

AMERICAN LARYNGOLOGICAL, RHINOLOGICAL AND OTOLOGICAL SOCIETY

The annual meeting of the American Laryngological, Rhinological and Otological Society will be held in Atlantic City from April 7 to 9 (secretary, C. S. Nash, M.D., 277 Alexander Street, Rochester 7, New York).

AMERICAN ASSOCIATION OF BLOOD BANKS

The annual meeting of the American Association of Blood Banks will he held in Buffalo, New York, from August 26 through 28, immediately after the meeting of the International Hematology Society there.

The American Association of Blood Banks was organized on November 19, 1947, at Dallas, Texas, to promote and foster the exchange of ideas and materials and the dissemination of information relating to blood banking and its technical methodology by education, publicity and research; to foster and plan for co-operation in times of disaster; to function as a clearing house on questions relating to the training of personnel common to such institutions; to keep currently aware of and encourage high standards of service; and to promote and foster the extension of similar services throughout the United States and its territories.

Membership in the Association is of two classes — an institutional membership is available to ethical, independently operating and policy-making, nonprofit institutions, including those operated by hospitals registered with the American Medical Association engaged in blood banking, and individual

memberships are open to any person interested in blood banking.

Requests for applications for membership or general information should be addressed to Miss Marjorie Saunders, LL.B., Secretary, American Association of Blood Banks, 3301 Junius Street, Dallas, Texas.

AMERICAN PUBLIC HEALTH ASSOCIATION

The seventy-sixth annual meeting of the American Public Health Association will be held in Boston from November 8 to 12 inclusive. Representatives from all parts of the United States, from Canada, Cuba and Mexico and from Latin American countries, as well as delegates from Europe and Asia, will attend. The following related organizations will hold their annual meetings at the same time and in the same place as the Association: American School Health Association; Association of Maternal and Child Health and Crippled Children's Directors; Association of Reserve Officers of the United States Public Health Service; Association of State and Territorial Health Officers; Conference of Municipal Public Health Engineers; Conference of Professors of Preventive Medicine; Conference of State and Provincial Public Health Laboratory Directors; Conference of State Directors of Health Education; Council of State Directors of Public Health Nursing; National Committee of Health Council Executives; and Public Health Cancer Association.

An extensive scientific program is in preparation, with particular attention to problems of public-health dentists, engineers, epidemiologists, food and nutrition specialists, health officers, industrial hygienists, laboratory workers, maternal and child health experts, public-health educators, public-health nurses, school health specialists and vital statisticians.

RESIDENCY IN PSYCHIATRY AT JOSEPH H. PRATT DIAGNOSTIC HOSPITAL

A new residency in psychiatry for one-year service is immediately available at the Joseph H. Pratt Diagnostic Hospital, Boston.

Service will consist largely of diagnosis and management of patients with neuroses and with personal and emotional complications of disease. Applicants should have an internship as a minimum of training.

In general residencies will begin on January 1 or July 1, except for the residency mentioned above.

Applications should be addressed to Mr. Richard T. Viguers, administrator.

MEDICAL ASSOCIATION OF THE STATE OF ALABAMA

The annual meeting of the Medical Association of the State of Alabama will be held in Mobile from April 15–17 (secretary, D. L. Cannon, M.D., 519 Dexter Avenue, Montgomery 4, Alabama).

ARKANSAS MEDICAL SOCIETY

The annual meeting of the Arkansas Medical Society will be held in Little Rock from April 15–17 (secretary, W. R. Brooksher, M.D., 602 Garrison Avenue, Ft. Smith, Arkansas).

CALIFORNIA MEDICAL ASSOCIATION

The annual meeting of the California Medical Association will be held in San Francisco from April 11–14 (secretary, L. H. Garland, M.D., 450 Sutter Street, San Francisco 8, California).

FLORIDA MEDICAL ASSOCIATION

The annual meeting of the Florida Medical Association will be held in St. Augustine from April 12–14 (secretary, Robert B. McIver, M.D., Box 1018, Jacksonville 1, Florida).

LOUISIANA STATE MEDICAL SOCIETY

The annual meeting of the Louisiana State Medical Society will be held in Monroe from April 12 to 14 (secretary, P. T. Talbot, M.D., 1430 Tulane Avenue, New Orleans 13, Louisiana).

TENNESSEE STATE MEDICAL ASSOCIATION

The annual meeting of the Tennessee State Medical Association will be held in Nashville on April 13 and 14 (secretary, W. M. Hardy, M.D., 706 Church Street, Nashville 3, Tennessee).

SOCIETY MEETINGS AND CONFERENCES

Calendar of Boston District for the Week Beginning Thursday, March 25

Friday, March 26

*9:00–10:00 a.m. The Distribution of Amino Acids between Cells and Extracellular Fluid. Dr. Halvor Christensen. Joseph H. Pratt Diagnostic Hospital.

*10:00 a.m.–12:00 m. Medical Staff Rounds. Peter Bent Brigham Hospital.

Monday, March 29

*12:15–1:15 p.m. Clinicopathological Conference. Peter Bent Brigham Hospital.

8:15 p.m. New England Heart Association. Beth Israel Hospital, Boston.

Tuesday, March 30

*12:15–1:15 p.m. Clinicoroentgenological Conference. Peter Bent Brigham Hospital.

*1:30–2:30 p.m. Pediatric Rounds. Burnham Memorial Hospital for Children, Massachusetts General Hospital.

Wednesday, March 31

*9:00–10:00 a.m. Radioactive Phosphorus Therapy. Dr. Bruce Brown. Joseph H. Pratt Diagnostic Hospital.

*12:00 m. Grand Rounds and Clinicopathological Conference. (Children's Hospital.) Amphitheater, Peter Bent Brigham Hospital.

*2:00–3:00 p.m. Combined Clinic by the Medical, Surgical and Orthopedic Services. Amphitheater, Children's Hospital.

*Open to the medical profession.

March 22, 24 and 26. Edward K. Dunham Lectures. Page 419.

March 23. Norfolk District Medical Society. Page 384, issue of March 11.

March 28–April 4. American Association of Industrial Physicians and Surgeons, American Industrial Hygiene Association, American Conference of Governmental Industrial Hygienists, American Association of Industrial Nurses, Inc., and American Association of Industrial Dentists. Hotel Statler, Boston.

March 29. New England Heart Association. Page 419.

March 30–April 1. American Association of Industrial Physicians and Surgeons. Page 419.

April 7–9. American Laryngological, Rhinological and Otological Society. Page 419.

April 7, 9, 14 and 16. American Trudeau Society. Page 240, issue of February 12.

April 8. Endometriosis. Dr. John Fallon. Pentucket Association of Physicians. 8:30 p.m. Haverhill.

April 10. American Congress of Physical Medicine. Page 344, issue of March 4.

April 12. Harvard School of Public Health. Page 384, issue of March 11.

April 13. Harvard Medical Society. Amphitheater, Building D, Harvard Medical School.

April 19–23. American College of Physicians. Page xiii, issue of July 31.

April 29–May 2. American Academy of Pediatrics. Page 240, issue of February 12.

May 6. Suffolk Censors' Meeting. Page 344, issue of March 4.

May 6–8. American Association for the Study of Goiter. Page xiii, issue of July 31.

May 16–22. American Board of Obstetrics and Gynecology, Inc. Page 344, issue of March 4.

May 16–23. International College of Surgeons. Page 136, issue of January 22.

May 17–20. American Urological Association. Hotel Statler, Boston.

May 18–22. American Association on Mental Deficiency. Copley Plaza Hotel, Boston.

May 20–25. American Board of Ophthalmology. Page 170, issue of January 29.

May 25–27. Massachusetts Medical Society. Annual Meeting. Hotel Statler, Boston.

June 21 and 22. American Society for the Study of Sterility. Page 384, issue of March 11.

June 28–30. American Academy of Pediatrics. Hotel Schroeder, Milwaukee, Wisconsin.

(*Notices concluded on page xix*)